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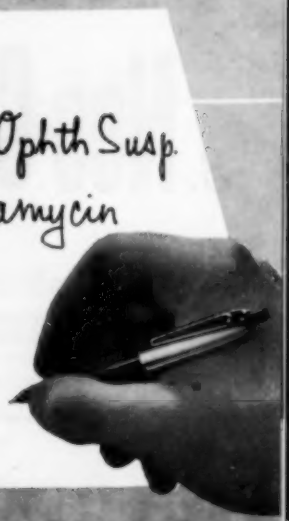

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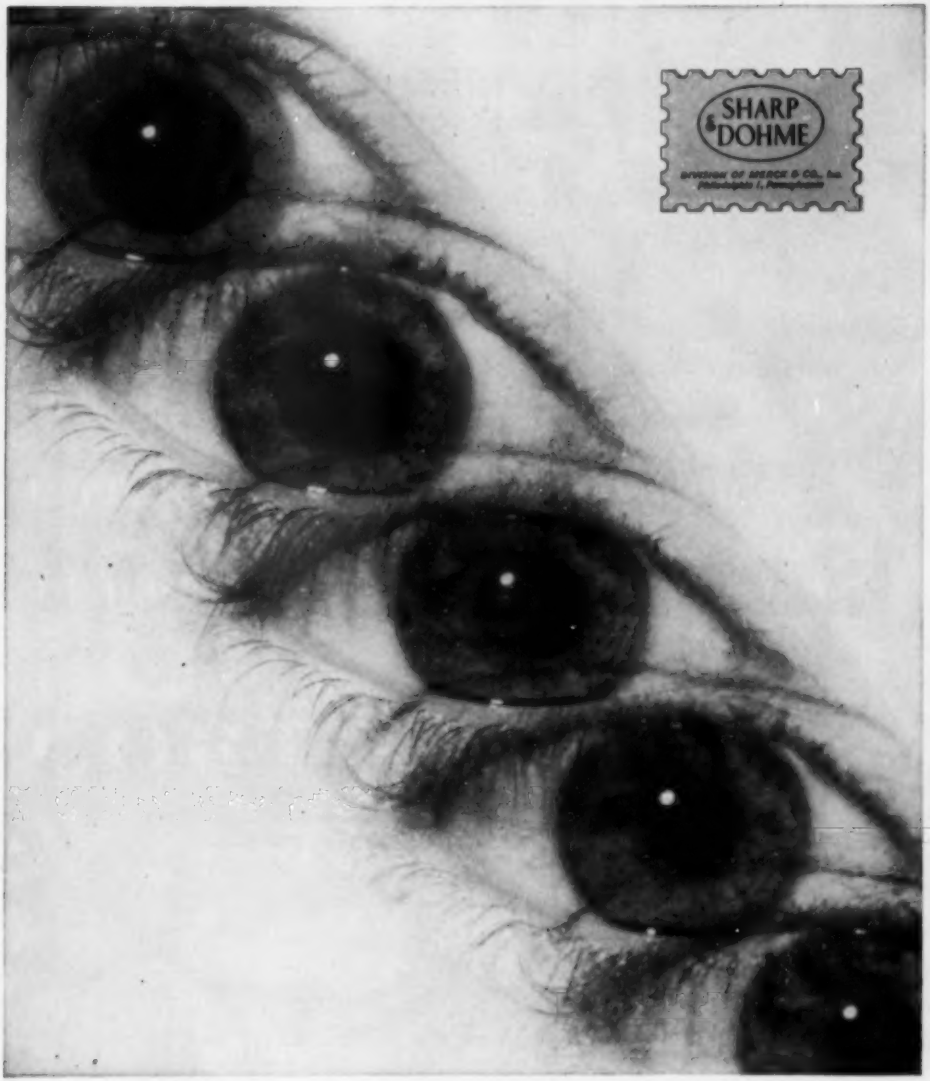

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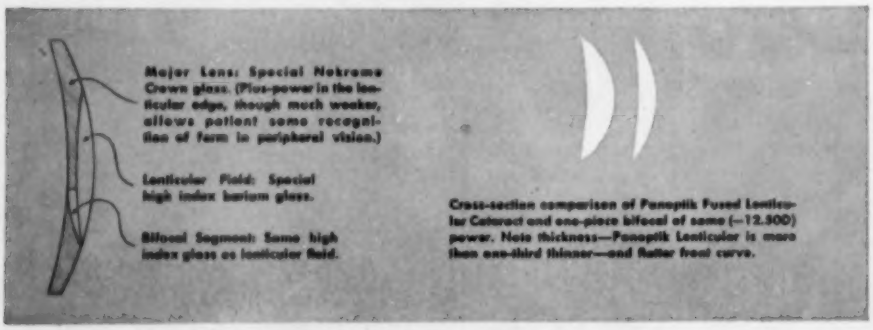
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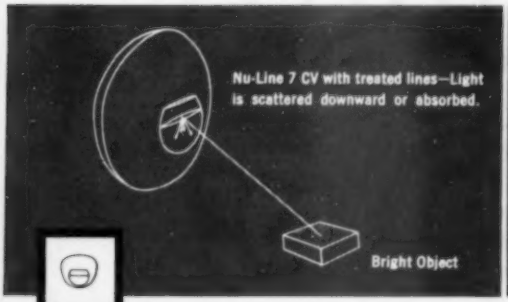

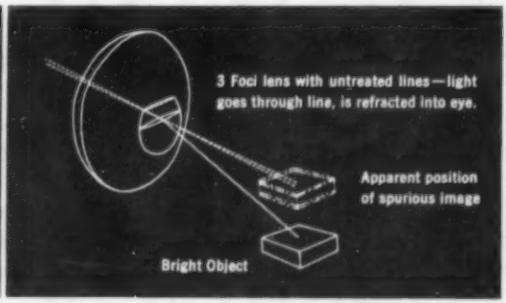
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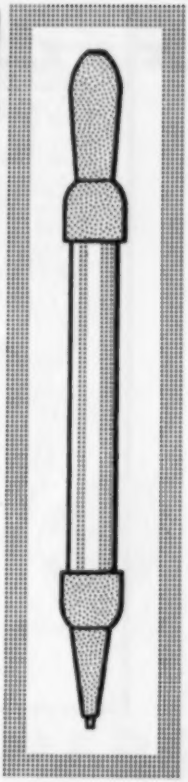

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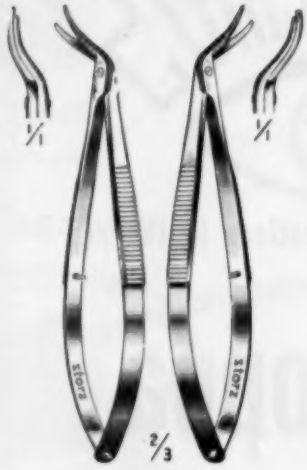

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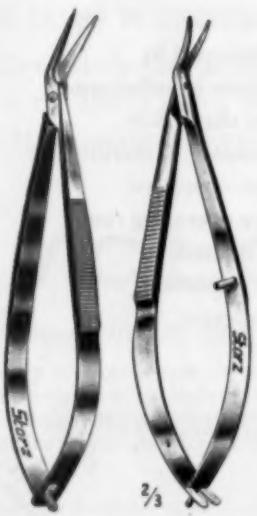

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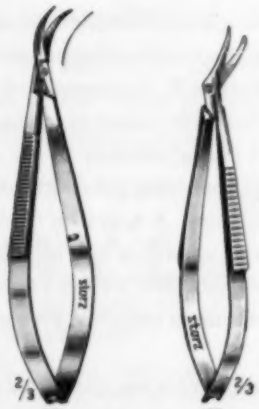

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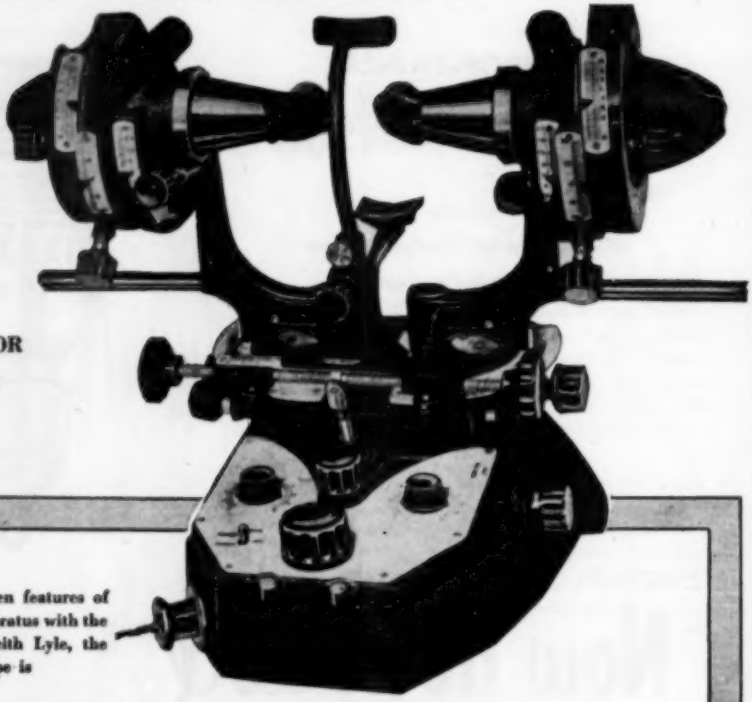

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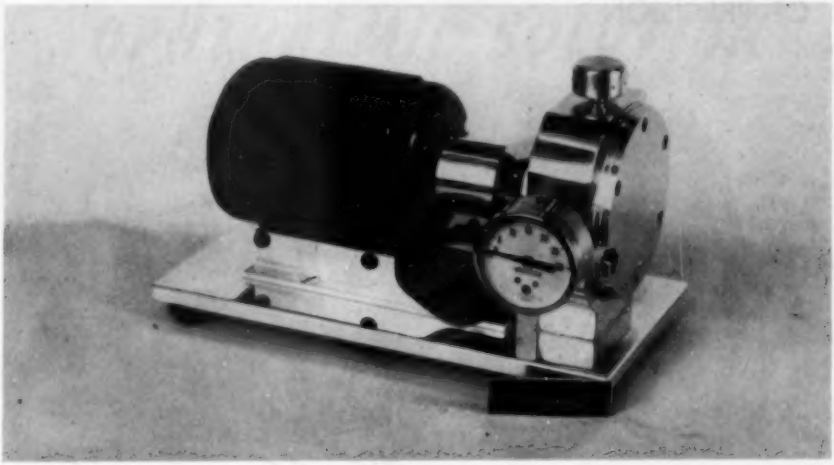

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"IF IT'S A LENS PROBLEM, LET'S LOOK AT IT TOGETHER"

AMERICAN JOURNAL OF OPHTHALMOLOGY

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ABSTRACTS

Physiologic optics, refraction, color vision; Diagnosis and therapy; Ocular motility; Conjunctiva, cornea, sclera; Uvea, sympathetic disease, aqueous; Glaucoma and ocular tension; Crystalline lens; Retina and vitreous; Neuro-Ophthalmology; Eyeball, orbit, sinuses; Eyelids, lacrimal apparatus; Injuries; Systemic disease and parasites; Congenital deformities, heredity; Hygiene, sociology, education and history 966

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VOLUME INDEX i

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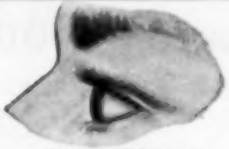

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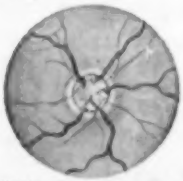

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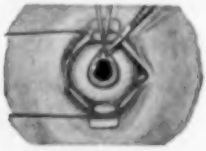

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VOLUME 37 JUNE, 1954 NUMBER 6

CLINICAL DETECTION OF THE GENETIC CARRIER STATE IN OPHTHALMIC PATHOLOGY*

THE JACKSON MEMORIAL LECTURE

HAROLD F. FALLS, M.D.
Ann Arbor, Michigan

This, the Jackson Memorial Lecture, is to honor the memory of a physician who contributed so much to establish the high stature enjoyed by American ophthalmology today. Dr. Jackson's was a constantly searching as well as an analytic mind, quick to seize and utilize even the most minute scientific detail if it could be employed to augment his own or his colleagues' diagnostic armamentarium. It is a singular honor to have been chosen to deliver this address and I am humbly appreciative.

The subject selected for this paper seems apropos, since it deals intimately with diagnosis and specifically with the clinical detection of the carriers of inherited ocular disease. Medical endeavor experiences cycles, just as there exist fads and modes in other fields of human enterprise. The modern physician, largely through the advent of antibiotics, chemotherapy, and preventive medicine, has slowly been forced to consider, with serious intent, the developmental, the degenerative, and the "inborn errors of metabolism."[5]

Medical science must again consider the patient as a whole and not from the viewpoint of isolated symptomatology. The constitution (that is, the sum total of the patient's hereditary potentialities and their intimate interrelationship with his environment) of the individual needs to receive the searching consideration of the alert ophthalmologist. In a sense this entire address is a plea to the oculist to devote constant study and research to, and to have a day-to-day awareness of, the role that "constitution" plays in ophthalmic pathology.

In a fairly strict sense, genetic carriers may be defined as individuals who possess the potentialities of transmitting inherited ocular disease, while they themselves show no or only a slight departure from normality. Neel and Schull[10] have most astutely classified genetic carriers into four chief categories as follows:

I. Individuals heterozygous for a pathologic trait which is commonly thought of as recessively inherited, but is actually due to an incompletely dominant gene.

II. Individuals having the gene for a disease trait which does not make its clinical appearance until late adolescence, or even middle or old age.

III. Affected individuals exhibiting only mild or minor effects of a dominant gene which, when transmitted to their progeny, may exhibit a more serious form.

IV. Carrier state for a large number of diseases in which the specific genetic mechanism is unknown, the carrier exhibiting clinically detectable departures from the norm, but which are relatively innocuous in character.

It will be most obvious to the audience that, given the tools by which to establish the diagnosis of the carrier state in these four

* From the Department of Ophthalmology, University of Michigan Medical School. Presented at the 58th annual session of the American Academy of Ophthalmology and Otolaryngology, October, 1953, Chicago, Illinois.

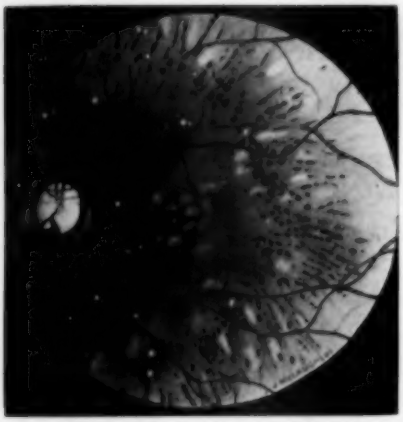

Fig. 1 (Falls). *Choroideremia.* Ophthalmoscopic appearance of typical female carrier state.

categories, we will be in an excellent position more accurately to predict the result of matings of such individuals. It is anticipated that early diagnosis, especially in category II, will enable us to combat and possibly prevent the later-appearing serious consequences of these diseases.

I. Individuals heterozygous for a pathologic trait which is commonly thought of as recessively inherited, but is actually due to an incompletely dominant gene

Diseases due to sex-linked intermediate genes

As our studies of hereditary ocular pathology have progressed it has become apparent that certain sex-linked genes are neither truly dominant nor recessive, but rather effect intermediate phenotypes in heterozygous females. Particularly is this true of a series of disease entities due to genes located in the x-chromosome. In this section, the following, arranged in the order of the clinical reliability of their detectable carrier state will be discussed: (1) "choroideremia"—progressive choroidal atrophy; (2) choroidoretinal degeneration; (3) sex-linked albinism confined to the eye; (4) keratosis follicularis spinulosa cum ophiasi; (5) congenital ophthalmoplegia; (6) megalocornea; (7) color vision anomaly, and (8) congenital anhidrotic ectodermal dysplasia.

"Choroideremia" — progressive choroidal atrophy. Largely through the combined efforts of Goedbloed, Waardenburg, the McCulloch's, and Sorsby and co-workers,[18] it has been established that "choroideremia" follows an intermediate gonosomal inheritance pattern. In the heterozygous females the choroideremia gene, located in the x-chromosome, presents an incomplete manifestation because of the ameliorating effect of its normal allelomorph. This heterozygous, or carrier female, presents a benign, stationary aberration of the retina and choroid, characterized by pigment granules, scattered irregular-sized areas of depigmentation, occasional circumpapillary atrophy, and no gross clinical alteration of visual physiology (fig. 1).

The male, in contrast to the carrier female, has only a single x-chromosome and the noxious gene has no normal allele to modify its effect. Progressive visual loss, night blindness, and visual field contracture may appear anywhere between extremely early childhood and 40 years of age. At first the ophthalmoscopic picture may resemble that of the carrier female, but eventually most of

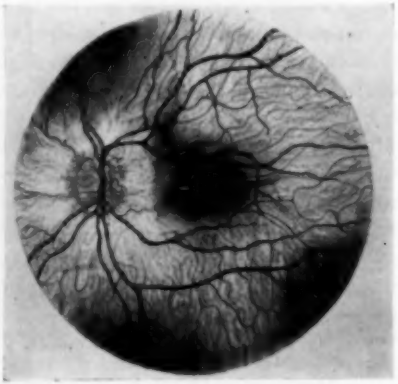

Fig. 2 (Falls). *Choroideremia.* Ophthalmoscopic appearance in a seven-year-old boy.

the choroidal vasculature atrophies and with it the retinal pigment and function. The optic nervehead and retinal vasculature retain a nearly normal appearance. The choroidal vasculature in the vicinity of the macula and the latter's pigmentation as well as function seemingly are more resistant to the atrophic process until fairly late in the course of the disease (fig. 2).

The detection of the typical carrier state in a sister or mother of the affected male will aid the ophthalmologist to establish the true diagnosis even in the earliest phases of the disease in the male.

Choroidoretinal degeneration. Falls and Cotterman[3] have described a probable variant of retinitis pigmentosa under the title of *choroidoretinal degeneration.* The affected males present evidence of primary retinal and choroidal degeneration of a progressive nature, having associated myopia and night blindness (fig. 3). The heterozygous, or carrier, female is most interesting in that she can be recognized by the presence of an ophthalmoscopic change best described as a tapetal-like reflex. A golden, glistening reflex can be obtained from the entire retina, but more concentrated in the posterior pole of the eye (fig. 4). These changes are probably the result of aberration in the thickness of the lamina vitrea. The carrier female does not exhibit any clinically detectable defect of visual acuity, night vision, or visual field.

Fig. 3 (Falls). *Choroidoretinal degeneration.* Ophthalmoscopic appearance of an affected male.

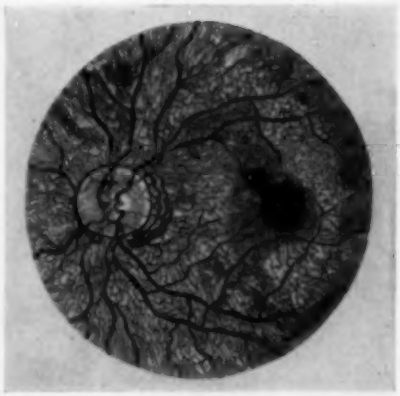

Fig. 4 (Falls). *Choroidoretinal degeneration.* Ophthalmoscopic appearance of a carrier female (tapetal reflex).

The significance of the presence of this carrier state is that its detection by the ophthalmologist permits him specifically to state that the affected female is capable of transmitting the gene to half of her male offspring and half of her female offspring, the males presenting "retinitis pigmentosa" with its usual course and prognosis and the females the clinically detectable carrier state.

Sex-linked albinism confined to the eye. Falls[3] has published evidence that a female carrier state exists in two families (two more families unpublished) which exhibit intermediate sex-linked ocular albinism. The affected males in these families eventually present normal skin and hair pigmentation. The irides are blue and diaphanous by scleral transillumination. The ophthalmoscopic picture is typically albinotic. It shows a varying degree of pinkness centrally, which extends peripherally in some males. This obscures, to some extent, the elsewhere prominent choroidal vasculature. The male state is further characterized by head nodding (present only in early life), amblyopia of varying

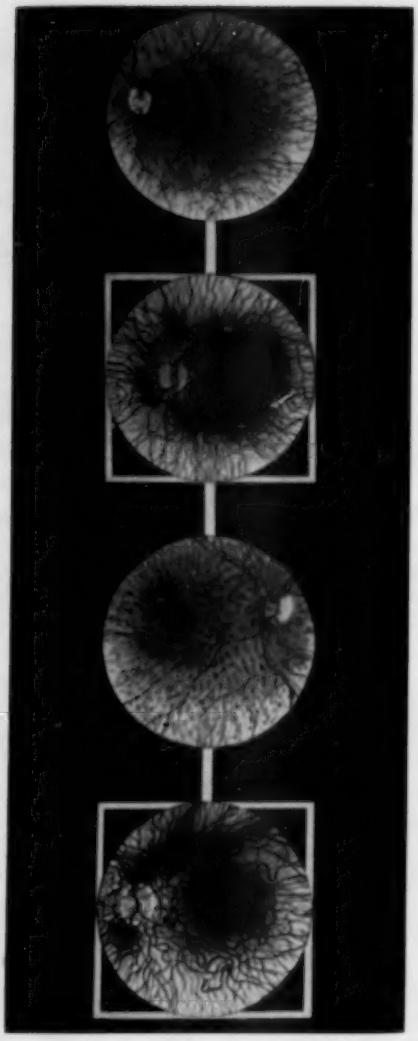

Fig. 5 (Falls). *Sex-linked ocular albinism.* Ophthalmoscopic appearance, in vertical representation from top to bottom, of a female carrier state and typical male retinal picture.

degree, and by nystagmus as well.

The carrier, or heterozygous, female presents normal skin, hair, and iris pigmentation. The ophthalmoscopic picture exhibits nearly normal pigmentation in and about the macular area. Within a disc diameter or so of the fovea, however, the pigment assumes a coarse, large, cocoa-brown, granular appearance, being arranged in little groups and islets (fig. 5). The choroidal vasculature may be seen with unusual clarity throughout the intermediate and peripheral zones of the optic globe. There is, therefore, an unusual sparsity of pigment throughout the entire fundus, but more specifically in the intermediate and peripheral retina. The visual fields and most phases of ocular physiology of the female carrier are apparently unaffected. Waardenburg maintains that all carrier females exhibit a diaphanous iris to scleral transillumination.

Keratosis follicularis spinulosa cum ophiasi. Siemens[13] (1925) presented to the literature a pedigree of keratosis follicularis associated with corneal degeneration. Women are apparently mildly affected in respect to the dermatologic changes, but exhibit no gross ocular changes. The affected men display alopecia, thickening of the eyelids, ectropion, loss of cilia, and a degenerative corneal pannus. Changes in other mucous membranes were sometimes encountered and the skin of the palms and soles was greatly thickened. Photophobia and epiphora were frequently exhibited.

It has been our experience recently to encounter a second family in which two brothers and their maternal uncle exhibited the typical male state and their mother the carrier, or heterozygous, state.

Congenital ophthalmoplegia. An interesting family exhibiting congenital ophthalmoplegia associated with myopia was reported by Salleras and de Zárate[14] (1950). The mode of inheritance of this entity was most probably sex-linked intermediate. The affected males presented complete bilateral ptosis, complete or incomplete ophthalmoplegia, strabismus, corectopia, dyscoria and anisocoria, myopia with progressive degenerative choroidal and retinal changes, and widely varying neurologic and physical defects. The carrier females in this family ex-

hibited consistent absence of the ankle and knee jerks.

Megalocornea. Megalocornea in the vast majority of cases has been transmitted by an x-chromosome located gene. Occasional heterozygous females[12] may exhibit megalocornea and when detected definitely constitute the carrier state.

A few rare pedigrees of megalocornea have suggested an autosomal dominant form of transmission. Affected females in the latter type of inheritance can in no way be differentiated from the rarely affected sex-linked heterozygous female other than by careful study of the individual family pedigree.

Color vision anomaly. Anomalies of color vision, deuteranopia, protanopia, and tritanopia, are inherited as sex-linked recessive traits. Affected females, homozygous for the x-chromosome gene, may be anticipated from matings involving a female carrier and an affected male; however, careful study of certain families occasionally discloses that clinically affected females do occur in whom the heterozygous state exists with full expression of the gene in the female. There is, furthermore, considerable evidence[11] that a number of females, heterozygous for the gene responsible for color vision anomaly, are not always completely normal in their color physiology. These mildly to fully affected females with color vision anomalies constitute the carrier state.

Congenital anhidrotic ectodermal dysplasia. A sex-linked recessive inheritance pattern exists for the entity known as congenital anhidrotic ectodermal dysplasia. The affected male exhibits anodontia, lanugo hair, ozena, lack of sweat glands, and occasionally absence of the lacrimal glands and cilia.[6] Heterozygous females may on occasion exhibit partial anodontia as well as anomalies of the sweat and mammary glands. Such females constitute the carrier state. A less severe form of the disease is inherited as an autosomal dominant in which the female is affected in equal proportion to the male. Meticulous pedigree studies are necessary to differentiate between these two types of affected females.

Diseases due to autosomal genes

A very large number of ocular disease entities exist due to autosomal "recessive" genes in which the heterozygote may occasionally exhibit varying manifestations of the single gene state. In other words, in that specific individual the gene is not entirely recessive to the normal allele and consequently effects the individual's resultant phenotype. It must be emphasized that the terms *recessive* and *dominance* are at best only relative states. The mildly affected heterozygote constitutes the carrier state.

Xeroderma pigmentosa. Xeroderma pigmentosa is characterized by the gradual appearance of large "freckles" on the exposed parts of the body. Later telangiectasia and subsequent epitheliomatous degeneration develop. The cornea and conjunctiva are frequently involved with a severe accompanying photophobia. The disease has been thought to be transmitted as an autosomal recessive, but recent evidence suggests that it is partially sex-linked.[9] The heterozygote, or carrier, state is characterized by permanent, heavy freckling and an occasional nevus formation.

Strabismus. Strabismus may be primary or secondary. In the latter, visual axis deviation may be the external manifestation of subtle central nervous system aberrations as well as a consequence of local ocular trauma, infection, or anomalous anterior segment development.

The role of heredity in the causation of primary strabismus has been well established by careful twin and family studies. These data support the conclusion that transmission of exotropia and esotropia, in the preponderance of families, is by an autosomal dominant gene having fair penetrance but exhibiting varying expressivity. Hyperopia need not be associated with esotropia nor myopia with exotropia, for indeed both may

be transmitted as independent characters. Amblyopia, according to both Sorsby[17] and Waardenburg, is a secondary feature and is not of itself genetically determined.

The carrier state of esotropia is fairly well established in that occasional individuals, heterozygous for the gene, may exhibit esophoria. It is, therefore, self-evident that careful muscle balance studies of the entire family being investigated must be meticulously performed.

Exophoria (in specific exotropia families) may possibly represent the carrier state of exotropia, but our experience indicates that the incidence of the condition in the general population is much too high for it to serve as a reliable manifestation of the carrier state of exotropia.

Juvenile amaurotic idiocy. Juvenile amaurotic idiocy, an affection of the central nervous system, is characterized by progressive visual loss occurring in young children, an increasing loss of sensory mental and physical powers, and eventual death at or about puberty.

A high rate of consanguinity and the multiple appearance of the disease in sibships suggest that an autosomal recessive gene is responsible for the trait. The frequent appearance of various mental and neurologic stigmata recurring in the relatives and antecedents of affected patients raises the question of occasional heterozygous (or simplex gene state) manifestation. The carrier state, according to Rayner[12] (1952), can be detected by the presence of an increased incidence of vacuolated lymphocytes in blood smears of heterozygotes for the trait.

Albinism. Generalized albinism actually presents a wide range of variation in the degree of absence of pigmentation in the skin, hair, and eye. In albinism the ocular associations include nystagmus, diaphanous irides, photophobia, amblyopia, strabismus, and errors of refraction.

In a previous paper it was suggested that several genotypes exist for generalized albinism, but most commonly an autosomal recessive gene is responsible. The carrier state, or heterozygote, may be detected, according to Waardenburg,[22] by scleral transillumination revealing the presence of a diaphanous iris.

Wilson's disease. Hepatolenticular degeneration is a chronic, progressive, and fatal disease of early adolescence. The chief pathologic findings are degeneration of the lenticular and caudate nucleus associated with cirrhosis of the liver. Tremor, rigidity, athetosis, impairment of voluntary movement, and loss of emotional expression are also present. The biomicroscopic study of such individuals frequently reveals the pathognomonic Kayser-Fleischer ring at the periphery of the cornea.

The frequency of consanguinity among the parents of the affected and the multiple occurrence among siblings suggests an autosomal recessive gene mode of transmission for the disease.

Uzman and Hood[20] (1952) have revealed that the preclinical homozygote may present abnormal or increased amounts of specific amino acids in their urine and thus this with, or possibly without, the Kayser-Fleischer ring constitutes the carrier state.

Keratoconus. Keratoconus has been reported as exhibiting both autosomal recessive and dominant modes of inheritance. In some pedigrees the carrier state may be detected by the presence of a "split shadow" upon retinoscopy or a high degree of astigmatism.[17]

Laurence-Moon-Bardet-Biedl syndrome. The essential components of the Laurence-Moon-Bardet-Biedl syndrome are (1) hypogenitalism, (2) primary retinal degeneration, (3) obesity, (4) mental deficiency, and (5) polydactyly. The retinal changes may simulate typical retinitis pigmentosa, retinal degeneration secondary to choroidal atrophy, or that of cerebromacular degeneration. These retinal changes constitute a key component of the syndrome.

The consensus at present is that the syn-

drome is transmitted by a recessive gene exhibiting considerable variability of expression. The common occurrence of neurologic and mental stigmata, polydactylism, deafmutism, and obesity among the antecedents of such patients must be interpreted as occasional expressions of the gene in the heterozygote state.[17] The minimal or partial manifestation of the syndrome constitutes the carrier state.

II. Individuals having the gene for a disease trait which does not make its clinical appearance until late adolescence, or even middle or old age

It is becoming increasingly apparent that heredity plays a most important role in a majority of the diseases of middle or old age. This is especially true of the degenerative and so-called stress diseases. The active ophthalmic physician soon becomes aware of the fact that each advancing decade carries with it an increasing incidence of glaucoma, hypertension, gout, and arthritis, as well as the degenerative diseases of the cornea, retina, and choroid.

It must be acknowledged that the ophthalmologist will seldom encounter the carrier state of the diseases in this category, especially essential hypertension, gout, and ankylosing spondylitis, but rather the ocular manifestations of the fully developed state. Yet if this same physician merely possesses an awareness of the genetic background of these diseases he will have gone a long way toward detection of their carrier states among the relatives of his affected patients.

Glaucoma. Primary glaucoma, one of the most serious of ophthalmic problems, has been reported to be a disease chiefly of middle and advanced age. In fact, according to some authorities, the greatest incidence occurs between 60 and 70 years of age. As a result of routine tonometry in our clinic we strongly feel that this age level of onset is much too high, since we are more and more frequently making the diagnosis in the late thirties and forties. Heredity plays an important role in the causation of primary glaucoma, both acute and chronic, but the exact mechanism by which the gene acts is yet unknown. Different genotypes may effect the same clinical picture. Thus each individual, as well as the involved family, must be interpreted in light of the specific pedigree of that family rather than from data obtained from pooled pedigree studies. A dominant autosomal gene for glaucoma with a varying degree of penetrance has repeatedly been reported. These data are strongly biased, since most studies have been initiated by discovering a young propositus whose antecedents are still alive for study. Most available material thus pertains to the entity known as juvenile glaucoma. There is, consequently, a great need for an intensive study of the hereditary influence in glaucoma states of later age onset.

The carrier state of primary glaucoma may be detected in relatively early life, in some cases, by the physician who possesses the previously mentioned awareness of the hereditary influence in the disease and who takes the time and trouble to examine the available relatives of his glaucoma patients. Tonometry and provocative tests are the tools in our armamentarium which enable us to establish the presence or absence of the disease *at the time* of the examination. Periodic or yearly examinations are urged for the relatives of glaucomatous individuals.

Essential hypertension. Impairment of vision may not infrequently be among the first of symptoms to influence the affected hypertensive patient to seek the services of the ophthalmic physician. The ocular ravages of essential hypertension in specific individuals are only too well known to this ophthalmologic audience and will not be reviewed. Modern medical and surgical advances have been achieved in the control of the hypertensive state. The preponderance of the available evidence favors the existence of an inherited

predisposition to the development of hypertension. The possibility of an autosomal dominant gene mode of transmission has received strong support. Careful history, ocular and physical examinations, and the cold pressor test of Hines and Brown[7] not infrequently reveal sufficient clinical data upon which the carrier state of essential hypertension may be detected. Hormonal and emotional stress phenomena, when more thoroughly understood, may reveal the basis for the development of more reliable detection tests in the future.

Again, as in glaucoma, the physician must possess an awareness of the role exerted by heredity and an interest in preventive medicine in order to initiate studies to uncover the carriers in the family of his affected patient.

Gout. Gout is a gene-determined disorder of uric acid metabolism chiefly affecting males. The rather rare ocular manifestations are intractable episcleritis and scleritis, chronic iridocyclitis, and conjunctival and corneal tophi. The genetics of gout are most intriguing. The tendency to hyperuricemia is due to an autosomal dominant gene.[16] The factor is expressed differently in the two sexes in that the postpubertal heterozygous males exhibit higher blood uric acid levels than the heterozygous females. Only 10 percent of hyperuricemic individuals develop gout. The basic cause for the manifestation of the clinical symptoms is still unknown.

A knowledge or suspicion of the existence of gout in the family of your patient warrants a repeated determination of the blood uric acid level.

Ankylosing spondylitis (*spondylitis rhizomélique*). It has been estimated that approximately 40 percent of the patients affected with ankylosing spondylitis will eventually exhibit chronic or acute nongranulomatous uveitis. The evidence in the literature for the role of heredity in the etiology of the disease, while not striking, is somewhat suggestive. It appears that a predisposition is questionably transmitted by a dominant gene having poor penetrance. This exhibits itself inconstantly in the female sex.

The oculist should be cognizant of this association of uveitis with ankylosing spondylitis. Careful roentgenographic studies of the lumbosacral and sacroiliac joints should aid in detecting the afflicted individual early in the course of the disease.

Fuchs' epithelial and endothelial dystrophy. The evidence for the role of heredity in the etiology of Fuchs' corneal dystrophy is admittedly scant but sufficiently suggestive to warrant including this entity. Evidence from one of our incompletely studied families suggests that the entity may be transmitted by an irregular dominant gene, exhibiting incomplete penetrance and having a greater penetrance in the female sex.

The carrier state of this eventually severe deterioration of the cornea is the appearance of centrally located corneal guttata. It is important that meticulous biomicroscopy be performed on the corneas of the relatives of patients with this entity. The presence of such guttata, detected in presurgical work-ups, should warn the ophthalmic surgeon to avoid traumatizing the corneal endothelium, since surgical damage to this layer may not infrequently initiate the appearance of the dystrophic state.

III. Affected individuals exhibiting only mild or minor effects of a dominant gene which, when transmitted to their progeny, may exhibit a more serious form

This category includes a tremendous range of pathologic ocular and systemic entities. The discussion will be limited, however, to those syndromes with which I have had intimate contact. A syndrome may be defined, in the sense referred to in this paper, as a gene-determined complex of constitutional signs and symptoms. In general, it is indeed rare to encounter all the manifestations constituting the specific syndrome in

one affected individual. In fact a meticulous study of the complete family is necessitated in order to exhibit the entire pleiotropic manifestations of the gene. *Formes frustes*, or minimal manifestations of any syndrome, will here constitute the carrier state, since such individuals are capable of transmitting the syndrome, in severe form, to their progeny. It must be acknowledged that it is nearly impossible to ascertain where the carrier state ends and the mild manifestation begins in the majority of the syndromes discussed in this section. Indeed many of the audience may take issue, justifiably, with my interpretations, but since this is a maiden voyage in our field I welcome the guidance of many pilots. The ophthalmic physician needs be thoroughly acquainted with the protean expressions of any specific syndrome in order to be able to recognize these mild states, or *formes frustes*. Infrequently the ocular feature of the syndrome may constitute the sole manifestation of the carrier state. A certain degree of caution is to be exercised, however, in that specific features of a constitutional syndrome may of themselves be independently transmitted traits in specific families. Ectopia lentis is an illustration of this phenomenon in that it may be a most constant feature of Marfan's syndrome, but it also is known to be transmitted as an independent autosomal dominant, or very rarely recessive, trait.

Phakomatoses

The organic neurocutaneous syndromes, collectively termed the phakomatoses, constitute von Recklinghausen's neurofibromatosis, Bourneville's tuberous sclerosis, Sturge-Weber encephalotrigeminal angiomatosis, and von Hippel-Lindau angiomatosis retinae. These syndromes manifest extensive neurologic and cutaneous similarities, are gene determined, and present an extreme protean range of constitutional departures from the norm.

Von Recklinghausen's neurofibromatosis. Neurofibromatosis is a developmental anomaly characterized by tumorlike aberrations of ectodermal origin, primarily those of the skin and nervous system. Organs of mesodermal origin occasionally may be involved. Cutaneous tumors and pigmentation, central nervous system involvement, and changes in the skeleton, endocrine system, and visceral organs have also been found. The ocular changes, to mention but a few, include hydrophthalmos, anterior chamber and iris defects, mulberrylike tumors of the optic nerve and retina, glioma of the optic nerve, pulsating exophthalmos, and scleral, orbital, and eyelid tumors. The most characteristic feature of the syndrome is comprised by the neurinomatous and fibromatous skin tumors associated with pigmentation.

A dominant gene manifesting irregular penetrance and variability of expressivity is responsible for a large proportion of the cases. Drs. Crowe and Schull[1] have suggested that the carrier state constitutes the appearance of at least six café-au-lait spots, each of which exceeds 1.5 cm. in broadest diameter. These alone, or in association with any of the ocular manifestations of the syndrome, should suggest neurofibromatosis to the ophthalmologist.

Tuberous sclerosis. Tuberous sclerosis is likewise a congenital developmental anomaly characterized by the appearance of tumorlike malformations of the organs of ectodermal and mesodermal origin. The classical syndrome comprises epilepsy and mental deficiency in association with changes of the skin, especially adenoma sebaceum. A great variety of visceral tumors have been associated in addition to the bone diseases, vegetative-endocrine disorders as well as various other congenital defects. The ocular manifestations may include adenoma sebaceum extending to the eyelids as well as tumors of the retina and optic nerve.

An autosomal dominant gene with marked variability of expression is most commonly responsible for the trait.

Adenoma sebaceum is probably the key manifestation of the disease and constitutes the carrier state. Isolated visceral or retinal tumors may suggest the diagnosis to the informed investigator.

The entities Sturge-Weber and von Hippel-Lindau disease are rarely encountered and consequently have not been studied as extensively. The possible carrier states of these entities, respectively, include trigeminal angiomatosis and angiomatosis retinae.

Marfan's syndrome

Marfan's syndrome, a most unusual association of anomalies, embraces a wide range of ocular, skeletal, general, and visceral aberrations. In general the afflicted individual presents a considerable increase in length, particularly of the digits of the feet and hands, with a decrease in breadth due to slenderness of the long bones. A conspicuous lack of development of fatty and muscular tissue is present. The ocular changes comprise ectopia lentis, hypoplasia iridis, miosis, and axial and lenticular myopia.

The syndrome is of genetic origin and an autosomal dominant mode of transmission is most frequently encountered.

The carrier state may consist of any minimal combination of the features of the syndrome (formes frustes). In our experience *ectopia lentis*, the most commonly observed ocular anomaly, and the elongation of the fingers, either in combination or singly, are the most reliable carrier state manifestations.

Waardenburg's syndrome

A rather recently recognized syndrome thoroughly described by Waardenburg consists of (1) lateral displacement of the medial canthi and lacrimal points; (2) a hyperplastic, broad, high nasal root; (3) hyperplasia of the medial portions of the eyebrows; (4) total or partial heterochromia iridis; (5) circumscribed albinism of the frontal head hair (white forelock); and (6) congenital deafness or partial (unilateral) deafness.

Meticulous pedigree studies have revealed that the syndrome exhibits a dominant autosomal mode of inheritance. Varying degrees of penetrance of the several component anomalies have been observed. The order of decreasing penetrance appears probably to be in the order (1) to (6) as listed above.[21] The carrier state of this syndrome, therefore, would consist of lateral displacement of the medial canthi and lacrimal puncta either alone or in combination with one or more of the other components.

Status Bonnevie-Ullrich

Certain congenital human anomalies of the head and extremities have been reported by Ullrich[19] (1949) as finding their embryologic explanation in the damaging pressure of wandering cerebrospinal fluid blebs. This mechanism had been previously shown by Bonnevie (1931, 1935) to be responsible for an inherited syndrome described in the house mouse by Bagg and Little (1924). Two principal anomaly complexes have thus come to be described under the title of "Status Bonnevie-Ullrich." One of these, which Ullrich believes to be attributable to an identical wandering bleb mechanism, consists of congenital cranial nuclear defects (especially abducens and/or facial paralysis), combined with various anomalies (chiefly unilateral) of the ear, ocular adnexa, muscles (mainly pectoralis defect), and extremities (especially the hands).

The role played by genetics in status Bonnevie-Ullrich, while suggestive, has as yet not been ascertained.

The carrier state for the ophthalmologist with a high index of suspicion would consist of the association of unilateral ocular anomalies (anterior segment and adnexa) and developmental aberrations of the hands.[19]

Ehlers-Danlos syndrome

This syndrome is characterized by (1) hyperlaxity and hyperextensibility of the joints, (2) hyperlaxity and hyperextensi-

bility of the skin, and (3) friability and fragility of the skin and blood vessels with breaking, splitting, and formation of hematomas and pseudotumors subsequent to the slightest trauma. The severity of these characteristics, as has been observed for most syndromes, may vary among different individuals and in sibships. The ocular anomalies associated with this syndrome may include (1) repeated ecchymosis of the eyelids, (2) elasticity of the skin of the eyelids, (3) absence of the puncti, (4) papyraceous scars of the eyelids, and (5) a smooth, rubbery feel of the eyelids.

The literature contains many references to the genetics of this interesting syndrome and by far the majority of the reports implicate a dominant mode of transmission of the entity. Johnson and Falls[8] have presented evidence that the homozygous state of this trait may be more severe and even semilethal in contrast to the highly variable but relatively mild expression in the heterozygote.

The carrier state, in my experience, consists of the presence on the forehead of papyraceous scars (covered with atrophic or finely wrinkled skin) associated with hyperelasticity of the skin of the eyelids.

Myotonia dystrophica

Myotonia dystrophica embraces a wide symptom complex consisting essentially of myotonia, atrophy of specific muscle groups, associated baldness, gonadal atrophy, mental deterioration, and progressive senility. Cataract is the chief ocular manifestation of this disease and has been reported to occur, with varying familial frequency, in 35 percent of affected individuals. If careful microscopy is performed, I am certain that this incidence would be nearer 80 to 90 percent. Beautiful iridescent anterior and posterior subcapsular dots are the typical early biomicroscopic findings. Tonic pupils may be observed.

The syndrome is transmitted as irregular autosomal dominant with a fair degree of penetrance and a varying range of expressivity. The carrier state, or heterozygote, can be detected with a fair degree of reliability by the ophthalmologist who has an awareness of the association of the subcapsular lenticular iridescent opacities.

Essential familial hypercholesteremia

Xanthoma tuberosum is a clinical entity characterized by hypercholesteremia, a tendency toward xanthomatous involvement of the skin, tendon tumors, and early serious cardiovascular disease. The essential feature of the disease, namely hypercholesteremia, is transmitted as a "single abnormal gene which is incompletely dominant to its normal allele"—an incomplete dominant trait. The presence of xanthoma tuberosum multiplex represents the homozygous condition for the inherited factor which, when present in the single gene state (heterozygous), effects only hypercholesteremia.[24] Certain families, however, exhibit considerable interfamilial variation in the degree of expressivity of the trait, and some heterozygous individuals may quite closely approximate the clinical manifestations of homozygotes in other families. It is thus always necessary to individualize on a study of both the patient and his respective family.

Xanthelasma (of the eyelids) may frequently be the ocular manifestation of both the heterozygous and homozygous state of the disease. The frequent serious cardiac involvement accompanying the disease entity warrants the expenditure of the time and trouble necessary to obtain blood cholesterol studies and thus uncover the carrier individuals.

Osteogenesis imperfecta (van der Hoeve's syndrome)

The cardinal signs of van der Hoeve's syndrome consist of (1) blue scleras, (2) bone fragility, (3) deafness (otosclerosis), and (4) hyperextensibility of the joints.

Seedorf (1949) found blue scleras in all of his patients, while bone fragility occurred in 61 percent, and deafness in 26 percent. The literature indicates that any one of the above-mentioned may be encountered as independent entities in specific families.

The disease is inherited, and an autosomal dominant gene having a pleiotropic effect is responsible for the syndrome.

The key component of the syndrome consists of blue scleras and their presence identifies the carrier.

Mandibulofacial dysostosis (Franceschetti's syndrome)

Mandibulofacial dysostosis, a distinct and independent clinical entity, is frequently recognized by the presence of a characteristic "anti-mongoloid" obliquity of the palpebral fissures and an S-shaped appearance of the lower eyelids. Other features of the syndrome are a fishlike physiognomy, colobomas of the outer third of the lower eyelids, hypoplasia of the squamous portion of the malar and zygomatic process of the temporal bones, hypoplasia of the mandible, malformation of the external ear and external auditory canal, deafness, macrostomia and blind fistulas, and prolongation of the angle of the mouth toward the ears.[4]

It has been postulated that a gene producing developmental inhibitory action, occurring at about the seventh week of gestation, chiefly affecting the facial bones derived from the first visceral arch, could account for most of the observed pathology.

Transmission of this syndrome is by a dominant gene which exhibits incomplete penetrance and a marked pleiotropism. The key component of the syndrome is the characteristic aberration of the lower eyelids (or eyelid), and this represents the carrier state.

IV. Carrier state for a large number of diseases in which the specific genetic mechanism is unknown, the carrier exhibiting clinically detectable departures from the norm, but which are relatively innocuous in character

The discussion under this category will be limited to diabetes mellitus and allergic diseases because of the time and space limitations. The carrier state of these entities will seldom be encountered in the office practice of the ophthalmologist, but they are discussed because the knowledge that a carrier state does exist enables the physician to instigate preventive and prophylactic medicine.

Diabetes mellitus

Diabetes mellitus, a disorder of carbohydrate glucose metabolism characterized by hyperglycemia and glycosuria, has a genetic basis but the exact mechanism (or mechanisms) is unknown. The trait is indeed of frequent occurrence in the general population and, as will be shown to be true for allergy, may be affected by many different genotypes. In fact certain pedigrees and pooled studies have suggested dominant as well as recessive (autosomal and sex-linked) modes of inheritance. It is not known if the ocular (that is, retinal and lenticular) complications of diabetes are genetically influenced.

The carrier state, or symptomatic individual, may occasionally be detected by abnormal glucose tolerance curves, especially if the precaution is taken to standardize the diet for a few days prior to the test. Twin studies, furthermore, have revealed a definite genetic association between clinical diabetes and abnormal tolerance curves.

Fajans (1953) has personally communicated that there is some evidence to suggest that the administration of 125 milligrams of cortisone 12 to 24 hours prior to a glucose tolerance test, in a patient prepared by special diet, may make more certain the detection of the carrier individual.

Allergic diseases

Allergic states are extremely common in the general population and it is most likely that multiple mutations have occurred, pro-

ducing many different genotypes responsible for the clinical symptoms. The genetics of the allergic ocular states have been incompletely studied so that it is unknown, according to Sorsby, whether or not purely ocular allergy constitutes a distinct genetic type. Weiner, Zieve, and Fries[23] have suggested an autosomal questionably recessive gene which when homozygous is responsible for prepubertal allergy and when heterozygous is represented by postpubertal affected individuals.

Migraine is frequently reported as constituting an ocular manifestation of allergy and is transmitted by an autosomal dominant gene. It is perhaps incorrect, actually, to include migraine in the allergic states since allergy is but one of the many trigger mechanisms capable of setting off the complex in a specifically susceptible constitution.

Summary

1. Utilizing the classification developed by Neel and Schull, the carrier states of genetically determined ocular pathology have been discussed.

2. Throughout the paper it has been emphasized that a high index of suspicion or awareness of the hereditary nature of the various ocular and systemic entities constitutes a prime requisite to detection of the carrier states of genetic ocular pathology.

3. Many clinically, apparently similar, genetic ocular entities have different gene transmission patterns (that is, dominant, recessive, and sex-linked modes of inheritance exist). This phenomenon makes it imperative that the individual as well as his specific family be carefully studied before giving genetic prognostication.

4. Many examples were given of the marked pleiotropic effect manifested by the gene or genes responsible for the syndromes. It was repeated, again and again, that the entire family or families be studied in order to disclose all of the signs and symptoms of the specific complex.

5. The opportunity of establishing prognosis, especially as to onset, course, and severity of the specific disease, may be the reward for spending a few minutes with the siblings and parents of your difficult diagnostic problems.

Conclusion

This paper has been presented to serve as an elementary introduction to the subject of the detection of the carrier state in genetic ophthalmic pathology. The horizon in this field is constantly broadening. The invasion, for example, of the biochemist into ophthalmic research is a most welcomed and needed event, since it is anticipated that by this marriage the clinician will become better informed as to the specific enzymatic or hormonal patho-physiology occurring in many of these diseases.

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MANAGEMENT OF THE PSYCHOTIC PATIENT FOR OCULAR SURGERY*

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The problem of anesthesia for intraocular surgery of the psychotic patient reaches more than usual proportions at the Medical Center because of the large psychiatric division visited by the eye service. Most of our surgical patients from the psychiatric division are senile psychotics with cerebral arteriosclerosis who are to undergo operation for cataracts. Experience with these patients suggests that to prevent the misfortune of irrational behavior on the operating table, less sedation, rather than more, is indicated. The following is a survey of the observations on senile patients which led to this conclusion.

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Elements of senility are frequently seen in elderly patients, yet only a small proportion of these patients are hospitalized as psychotic. The question of hospitalization depends very much on the degree of environmental support available. A devoted son or daughter can protect the senile person from the dangers that may threaten him through his deteriorated mental condition. From long experience, members of the family can often intuitively foresee the onset of irrational behavior, and forestall or protect against its consequences. As a result, only a few, and not necessarily the most deteriorated of the senile psychotic population, are seen in psychiatric hospitals. The ophthalmologist in private practice must frequently deal with

these patients, especially in connection with the treatment of cataract.

Senile psychosis is easily recognized. Most characteristic is the loss of recent memory: the patient tends to forget recent experiences or conversations; he is apt to wander off and become lost. Remote memory is often well maintained, however, and the patient may remember the address of his childhood home, and particulars of public figures of years ago, while being unable to remember the current year or the name of the president.

Another characteristic of senile cerebral degeneration is deterioration of judgment, which may have serious consequences. For example, the patient may drop lighted matches and cause a fire. Control of the emotions disappears, and the patient seems self-centered and stubborn, and gives way to temper tantrums. Speech is usually coherent, but often irrelevant. In the more advanced stages, intellect is grossly lacking, and the person becomes disoriented and confused.

Translated into terms of analytic psychiatry, the senile patient has suffered a loss of *ego* strength. It is the ego which enables one to deal effectively with his needs, through such functions as judgment and memory. In the senile patient, the strength of the ego is greatly diminished, and the *super*, or parent, ego, which is in a sense the person's will to behave, is also lacking.

The threat of this symptom complex to ocular surgery, with the patient to a greater or lesser degree awake, can easily be appreciated. Lack of judgment makes it difficult for the patient to realize the value of the procedure and the danger of sudden, erratic movement on the operating table. Faulty recent memory may cause him to forget from one moment to the next that he is, in fact, being operated on, and a deteriorated super-ego structure leaves him without the will to co-operate for his own good.

All of our senile psychotic patients are evaluated by psychiatrists. It would seem, however, that for the purpose of selecting cases for ocular surgery, an ophthalmologist can successfully evaluate the average senile patient. The following method of approach should, it is felt, be utilized by the surgeon even if a psychiatric consultation is available:

Method of approach

Selection of the case hinges on the quality of the patient's *reality judgment*. This is conveniently tested by discussing the proposed operation directly with the patient. During discussion, the ophthalmologist should satisfy himself concerning the following questions:

1. Does the patient realize his visual disability and value its being improved?

2. Does he have appropriate regard for the seriousness of the procedure?

If judgment is adequate, the patient will show much concern, even exaggerated concern, at the prospect of surgery. He may forget all about it in 10 minutes, but more important is the fact that he can momentarily be made to understand, as proved by his appropriate response.

At subsequent examinations the patient's memory can be tested by questioning him about the previous discussion and plans. Memory is not as important as the judgment faculty, however, as it can when necessary be reinforced by the surgeon.

In no event does it seem wise to discuss only with the patient's relatives an impending procedure to be done under local anesthesia. The patient should never be deluded into thinking that only a minor, unimportant procedure is going to be done.

The patient who, on preliminary examination, shows deficient reality judgment is best deferred as a surgical risk. If surgery must be undertaken in these patients, the operation should probabaly be done either under general anesthesia, or by administering curare in conjunction with minimal sedation. With the use of curare, the patient remains conscious, but his motor activity is so weakened as to make sudden movement impossible. While it requires the presence of an anesthetist, it may well prove to be the method of choice with the more psychotic

patient. It is, however, with patients who are to be operated under the usual local anesthesia with whom we are here concerned.

The pathology of cerebral arteriosclerosis shows destruction of the cyto-architecture of the brain, with great diminution of brain cells, particularly of the neocortex. This is significant, firstly because the activity of the neocortex is further reduced by hypnotic drugs, and secondly because it is in the neocortex that the higher functions of the ego, already discussed, are affected.

Thus, while the patient who is not suffering from organic psychosis retains sufficient ego strength to co-operate during operation, even when heavily sedated, the senile patient's reserve of ego strength is so small that an equal amount of sedation will destroy it almost completely. In view of these facts, it is suggested that the principle of "the more psychotic, the more sedation," be discarded.

Operative management

On the nonpsychiatric eye service at the Medical Center, the average cataract patient receives preoperatively 0.2 gm. of Nembutal and 100 mg. of Demerol. Half of these dosages seems a safe maximum for the senile patient. At the table the patient is allowed as much contact with the surgeon as possible. His questions are answered and, if they seem inappropriate, he is reminded that the person speaking to him is the doctor, and that he is on an operating table having an operation performed upon his eye so that he will see better.

Whenever possible, prior to section, all reasonable requests, such as requests for more breathing space, or scratching of the nose, or requests for water, are fulfilled rather than frustrated. If the demands are not feasible, it is explained to the patient why they cannot be granted, and he is again reminded that he is being operated on.

The patient's requests, if unreasonable, are taken as a warning of waning reality judgment. Understanding the dynamics of the patient's deficiency, the surgeon can reinforce the patient's judgment, by reminding him of reality. This is somewhat similar to what the intuitive relative may do in the home situation.

Such control of the patient by the surgeon is only possible, however, if (1) there is sufficient judgment left to reinforce, and (2) this function has not been wiped out by excessive hypnotics and analgesics, such as Amytal and Demerol.

It has been our experience that an attempt to deal with irrational behavior on the operating table by further administration of drugs is unlikely to succeed, and may lead to disaster. If a dose of 7.5 gr. of Amytal is given, the patient is momentarily put to sleep, but he will reawake with the restarting of the procedure and is then totally beyond rational recall. His excitement upon awakening tends to be of even grosser proportions than prior to administration of the drug. Perhaps it is significant that some experimental work on the barbiturates indicates that while depressing cortico-efferent fibers, cortico-afferent fibers are much less affected. This may be the reason why the patient reawakens so easily.

Intravenous Demerol is the more desirable alternative because of its analgesic action; but its depressant action produces the danger of approaching uncontrolled general anesthesia without the usual precautions of providing an airway, and so forth. Further, like the barbiturates, it depresses cortical function to the point at which it is no longer possible for the surgeon to control the patient.

Summary

To summarize, it is felt that patients selected on the basis of an adequate reality judgment function can be dealt with most effectively with minimal sedation and analgesia, the surgeon maintaining psychologic contact with the patient during operation. Administration of additional and excessive hypnotics and analgesics on the operating table is an indication of poor selection.

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GLAUCOMA AND ELECTROSHOCK THERAPY

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Hibbeler,[1] in 1947, reported that patients with primary glaucoma more frequently have personality disturbances than unselected clinic patients. Male patients show a trend toward depression and hysteria; females toward paranoia and schizophrenia. It seems reasonable to assume that some of these patients will eventually require electroshock therapy.

The studies in the literature regarding electroshock therapy and intraocular pressure were all made on nonglaucomatous patients and contraindications are not clearly defined.

In 1948, Ehrhardt[2] reported a drop in tension following completion of the electroshock seizure of between 25 to 55 percent of the normal tension, with a rise in an hour or two. In 1950, McClellan, Markson, and Mills[3] found just the opposite, that is, a decided increase in tension during electroshock therapy with an adjustment to normal within two to three minutes after termination of the treatment. Arstikaitis and Hodgson,[4] in 1952, working with 21 nonglaucomatous patients found a sharp rise in tension in 18 after electroshock therapy and no change in the others. Tension returned to normal in about 30 minutes.

Most ophthalmologists and psychiatrists feel that glaucoma is a contraindication to electroshock therapy but no definite reason for this was found in the literature.

Both Kalinowsky,[5] and Sugar, author of *The Glaucomas*, in personal communications, said that they had had no experience with electroshock in glaucoma.

Electroshock therapy is a life-saving procedure in suicidal patients and, in such cases, one may be forced to take the chance of precipitating an acute glaucoma attack. After having to give electroshock treatments to a glaucoma patient, we decided that some information on the possible consequences was very much needed.

CASE REPORT

N. B., a 57-year-old married white woman, who had for the previous four years been treated for neurasthenia with abdominal complaints, anxiety, sleeplessness, and nervousness, began to complain of pain in her left eye on July 26, 1952. Tension was found to be: O.D., 30 mm. Hg (Schiøtz); O.S., above the limits of the tonometer. The increased tension was controlled for two days with Floropryl; then the right eye became hard and painful and could not be controlled medically. A complete iridectomy under local anesthesia was done on the right eye on July 30, 1952. The eye healed uneventfully and was asymptomatic. Tension in the left eye remained at 20 mm. Hg under Floropryl.

On August 16, 1952, the unoperated left eye became painful. Tension was 70 mm. Hg. A complete iridectomy was done on this eye on August 18, 1952, under general anesthesia because of the patient's extreme nervousness. The eye healed uneventfully, was asymptomatic, and pressure remained at 20 mm. Hg.

During both hospitalizations and at home, the patient complained of insomnia and extreme nervousness in spite of large doses of sedatives. On August 28, 1952, the patient was found to be confused, had lost considerable weight, and exclaimed continually that she wished she were dead. A diagnosis of involutional psychotic reaction, depression, and agitation was made. It was felt absolutely necessary to treat this patient with electroshock.

On August 30, 1952, she received the first electroshock treatment under Tubocurarine and was given 1.0 cc. Tensilon im-

mediately following the convulsion. Intraocular pressure prior to and immediately after electroshock remained within normal limits varying between 20 to 27 mm. Hg (Schiøtz). After receiving a total of six electroshock treatments between August 30 and September 14, 1952, she was considerably improved and had gained 12 pounds in weight. On February 16 and February 22, 1952, she received maintenance electroshock treatments. The intraocular pressure continued normal.

Discussion

At the annual meeting of the Iowa Academy of Eye, Ear, Nose, and Throat in November, 1952, a case of glaucoma was reported which had been controlled by surgery prior to electroshock therapy, but afterward the glaucoma could not be controlled by medical or surgical means and the eye eventually had to be enucleated.

The following eight cases were reported to us in personal communications:

Dr. Eugene M. Blake: The following are two cases that I thought might be of interest to you:

C. M., a research assistant, aged 30 years, was first seen November 12, 1936. Her mother had chronic glaucoma. Congestion of globe was present with tension of: R.E., 25 mm. Hg (Schiøtz); L.E., 25 mm. Hg. She developed a maniac depressive episode in 1947. Electroshock was given and she made a good recovery mentally and carried on her work in the library of a university as before. On December 4, 1952, tension was: R.E., 18.5 mm. Hg; L.E., 15.6 mm. Hg (electronic tonometer). Fields are intact.

F. N. was first seen July 19, 1920. The left eye was amblyopic. Vision with correction was: R.E., 20/20; L.E., 20/200. Tension was: R.E., 75 mm. Hg (Schiøtz); L.E., 24 mm. Hg. An acute congestive glaucoma occurred in the left eye in December, 1947, and scleroiridectomy was performed. The patient developed a maniac depressive episode in November, 1948. Electroshock was given, with good recovery. At semiregular examinations, no mental symptoms were noted. The last visit was September 5, 1952, when vision with correction was: R.E., 20/15; L.E., 20/100−1. Tension was: R.E., 25.4 mm. Hg.; L.E., 21 mm. Hg (electronic). She was mentally clear. The visual fields held.

Dr. John F. Gipner: I recently had a patient with chronic simple glaucoma, well controlled with miotics, who was given a course of electroshock therapy with no bad effects on the course of the glaucoma.

Dr. Alston Callahan: I have seen one case of secondary glaucoma following chronic uveitis in which a glaucoma operation had to be performed. The patient had some mental aberration and later received shock therapy. I do not know whether it was a recurrence of the uveitis or the physical trauma of the electroshock, or what the cause, but it was necessary to remove the eye.

Dr. Edwin B. Dunphy: I know of one patient with chronic simple glaucoma of the wide-angle type who developed a mental condition which required electroshock therapy. The course of the glaucoma was not affected by this therapy. The glaucoma had been controlled by miotics and is now so controlled.

Dr. Robert W. Mather: I have used electroshock therapy on one individual who had chronic congestive glaucoma. In this case, the application of the shock stimulus was followed by the usual reduction in ocular tension. No curare was used.

Dr. Ivan J. Koenig: Mrs. B. S., who received the diagnosis of glaucoma on her first visit, September 19, 1942, has had several flare-ups since that time. The glaucoma is the narrow-angle type. Her corrected visual acuity was: R.E., 20/20; L.E., 20/200. Tension has been controlled with miotics during this period. The fields have remained about the same. She was admitted to a nursing home for shock treatments on January 1, 1951, and remained about three months. The tension has since been under control with one-percent pilocarpine, three times daily.

Electroshock seems to have had no effect on her glaucoma.

DR. KENNETH C. SWAN: I have had one patient with narrow-angle glaucoma who received electroshock therapy for a depressive state. He had a functioning filtration operation in one eye, but in the other he received regular instillations of pilocarpine. As I recall, he had two electroshock treatments without ill effects on his glaucoma.

Since 32 eye departments of the medical schools contacted had had no experience with glaucoma and electroshock, it would seem that fewer glaucoma patients than one would expect, undergo electroshock therapy and very little seems to be known regarding complications. Although only 10 cases, gathered from various sources, are reported herein, the fact that the glaucoma condition recurred or was aggravated by electroshock therapy in two (20 percent) should certainly make one hesitate to recommend electroshock therapy in glaucoma patients, even when the glaucoma is well controlled.

SUMMARY

A case of glaucoma in which a mental condition made electroshock therapy necessary is reported in detail and nine other cases collected from various sources are summarized. Thirty-two medical school eye departments reported no experience with this combination of problems. Two of the 10 glaucoma cases became worse after electroshock therapy. This seems to indicate that the procedure is not without danger in glaucomatous patient. Further studies of this subject should be made.

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INFLUENCES OF CURARE AND ESERINE ON OCULAR TENSION FOLLOWING ELECTROSHOCK*

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INTRODUCTION

Interest in the study of aqueous-humor dynamics continues. Our knowledge of the blood-aqueous barrier and factors affecting the rate of flow of the aqueous was rapidly expanded with the contributions of Kinsey.[1] According to recent views, intraocular pressure is the resultant of the constant inflow and loss of fluid from the eye, this pressure being governed by hydrostatic and osmotic forces.

The factors[2] of significance in maintaining intraocular pressure under steady-state conditions are several, including: (1) The rate of outflow of fluid, (2) osmotic pressure differences between aqueous humor and blood,

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(3) the rate of aqueous-humor formation, and (4) the hydrostatic pressure, which appears to have little influence.

Some interesting observations on ocular-tension variations following electroshock therapy may be of significance in obtaining a better understanding of the physiologic processes underlying this important function. Our interest in this problem was initiated by the observation of a marked and persistent drop in ocular tension in a glaucomatous diabetic patient following an insulin-induced shock associated with convulsions. The present study was conducted in an effort to evaluate further the effects of convulsive shock therapy upon ocular tension and to observe the influence of various agents upon the resulting changes.

Previous work reported by Ehrhardt[3] demonstrated a decrease in ocular tension following electroshock. The fall in tension was maximal in five to 20 minutes with a return to normal within one to two hours. McClellan and others[4] reported a decided increase in ocular tension of curarized patients followed in several minutes by a rapid decline to preshock levels. The present observations may help in explaining these discordant results.

The effect of osmotic interrelationships between the aqueous humor and plasma as a factor in governing the rate of flow of the aqueous has recently been recognized.[1, 2] Changes in osmotic pressure induced by intravenous hypertonic sorbital, exercise, or the ingestion of large quantities of water are well known to affect ocular tension. Recently[5] it has been clearly shown that electroshock will result in transient changes in the osmotic gradient between intracellular and extracellular fluids. The present study suggests that variations in ocular tension following electroshock may be the consequence of these alterations.

Methods and Materials

Patients were selected from those under treatment with electroshock therapy in the Department of Psychiatry for psychoneurosis and depressive psychosis. The patients were free of ocular disease and were able to co-operate for the study. Tonometric readings were performed prior to the application of electroshock, pontocaine anesthesia being employed. The electroshock was administered with a standard, model B24, electroconvulsive therapy unit (Medcraft Electronic Corporation) having a glissardo control for a period of 0.85 seconds at +120 to +150 volts.

Tonometry readings were recorded at intervals of every one to two minutes during the clonic phase in most subjects, except in the first group studied, and every three to 10 minutes of the postconvulsive phase for a period of 30 to 70 minutes. In order to avoid altering ocular volume, a short application of the tonometer was employed.

The patients were divided into three groups:

Group I

These patients received electroshock only. A total of 34 eyes was examined in this group. The phenomenon of conjugate laterosuperior rotation of the eye during the clonic phase, described by Kino,[6] prevented accurate measurements during this interval in some of the patients.

Retraction of the lids with Desmarres retractors was performed unilaterally in 10 of the patients in this group. This was done during the tonic and clonic phases in order to evaluate the changes in ocular tension between the two eyes secondary to contraction of the orbicularis oculi muscles.

Group II

The second group of patients (11 eyes) received curare, administered intravenously as tubocurarine in dosage of 20 units per 40 pounds of body weight. In a few minutes, when the patient was unable to raise his head voluntarily, electroshock was given.

Ocular tension, prior to shock therapy, was slightly reduced following the intravenous curare in five of the eyes in this group. The curare was found to reduce the intensity of the convulsion by approximately one-third.

As in Group I, tonometric readings were carried out at frequent intervals after electroshock. The conjugate movement of the eyes was not observed after curarization.

Group III

The third group of patients (13 eyes) was given one-half percent eserine salicylate drops one in each eye every 10 minutes for five doses. This was followed by intravenous curare and, in a few minutes, the shock stimulus was applied.

Changes in ocular tension of eserinized eyes following intravenous curare did not exceed four mm. Hg. Significant changes in ocular tension were noted only after the application of electroshock.

The accuracy of the tonometric readings is influenced by the state of the patient following electroshock. Satisfactory readings can best be obtained during the period of postconvulsive stupor. When the patient is abruptly aroused from this state, he is temporarily unco-operative and may be somewhat manic, so that further observations of ocular tension cannot be accurately made. This phenomenon does not appear if the patient is permitted to emerge gradually from the postconvulsive stupor.

Blood-pressure recordings were obtained before, during, and after electroshock using a mercurial sphygmomanometer. Preliminary studies of serum sodium, potassium, chloride, and specific gravity of whole blood and plasma were initiated but will not be reported here.

Results

In the preliminary study, the constant finding noted after the application of electroshock was a reduction in ocular tension. This effect was observed in each of the 34 eyes in Group I. The ocular tension began to rise gradually thereafter, reaching preshock levels within the next seven to 70 or more minutes after the maximal drop.

The variations of ocular tension encountered in Group I are represented in Table 1. Measurements were not made consistently within the first three minutes because of the conjugate deviation; however, in several patients in whom this deviation was less pronounced and immediate postshock readings were attempted, the findings suggested a rise in ocular tension prior to the fall. The inability to obtain accurate readings in this phase does not permit satisfactory evaluation of the data obtained in these few cases. Unilateral lid retraction performed in 10 patients for the evaluation of the effect of blepharospasm disclosed no difference in the pressure changes in the two eyes thus eliminating one of the mechanical factors which may have been suspected as causing the drop in pressure.

In the curarized patients, Group II, there was a marked rise in ocular tension immediately after the onset of convulsive movements. This rise became maximal within two to three minutes after the electroshock stimulus. Due to technical factors, in some instances the tonometer weights were not changed when the scale indicator passed the zero mark. Therefore, increases in ocular tension above 44 mm. Hg were not recorded in certain of these cases.

With the exception of two eyes in which the ocular tension remained moderately elevated for at least 12 minutes after electroshock, the ocular tension in this group promptly declined to preshock levels within approximately five minutes and showed no further variation. Tonometry could be accurately performed in the tonic and clonic phases because of the absence of conjugate rotation. The variations of ocular tension encountered in Group II are represented in Table 2.

TABLE 1

VARIATIONS IN OCULAR TENSION IN GROUP I

(Measurements of ocular tension following the administration of electroshock therapy.)

SCHIØTZ

Eyes Odd=right eye Even=left eye	Ocular Tension Before E.S.T.	Shock Stimulus	Minutes																												
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	30	45	60	70
1	23						10					19					22															
2	24						12					15					20															
3	27						14					14										20							21			
4	25						14					14										20							20			
5	28			28			21			20		24					28															
6	28			28			15			20		22					28															
7	20					11								20																22		
8	19					11								20																20		
9	21						10							20																		
10	21						10							20																		
11	26						17			20																			20	17	17	14
12	27						12			17																			21	17	16	17
13	20				10					10					12						15								14	13	
14	18				10					12					12						17								12	10	
15	27					17				17												27									
16	27					17				18												27									
17	23						14																								
18	20						14																								
19	22						10					15					20					22										
20	21						10					15					19					20										
21	27					12																							24			
22	26					12																							27			
23	18					14		14		10			8				18							20								
24	20					17		14		12			8				18							20								
25	27						15					20																				
26	26						17					21																				
27	20														20								19				16	15		20		
28	20														17								16				13	11		18		
29	20						14																									
30	20					17				14				16								18							18			
31	21									20																	15	13	17	21		
32	18									19																	14	12	15	19		
33	20							17						18												21		21				
34	20							15						18												21		23				

TABLE 2

VARIATIONS IN OCULAR TENSION IN GROUP II

(Measurements of ocular tension in curarized patients following the administration of electroshock therapy.)

	Eyes Odd=right eye Even=left eye	Ocular Tension Before any medication	Ocular Tension 1–4 min. After I.V. Curare	Shock Stimulus	Minutes 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	25	30
SCHIOTZ	1	19				32	50			35		38				30						22				
	2	19				32	43			43		40				32						24				
	3	30	26			44*					29			27								25				
	4	24	24			44			24																	23
	5	27	27			44			26																	25
	6	29	27			44*			28					28												
	7	27	26			44			27					26												
	8	23	19			34			29				20				20									
	9	20	19			45			29				20				20									
	10	28	28			56				28				28					28							
	11	28	28			58				29				29					29							

* Rise of ocular tension above 44 mm. Hg, i.e. beyond zero mark on Schiøtz scale.

In Group III, the effect of eserine applied locally to the eyes modified the postshock tension variations observed in Group II. Following the electroshock stimulus in the eserinized-curarized patients, a marked increase in ocular tension was observed which was comparable to that seen with curare alone.

The rise occurred within two to four minutes. This was followed by a progressive fall below the preshock levels as was observed in the Group I patients who had not received curare. However, in this group, the maximal decline was delayed until nine to 12 minutes after the shock stimulus. Following this biphasic response, the ocular tension returned toward the preshock levels. These variations are depicted in Table 3.

DISCUSSION

The observations recorded here demonstrate that following electroshock there is a rapid drop in ocular tension. This drop is replaced by a rise in tension in patients given curare prior to shock and is again observed in the eserinized-curarized patients after a preliminary rise.

One explanation offered for the decrease in ocular tension following electroshock has been that of compression of the globe with expulsion of fluid from the eye secondary to contraction of extraocular muscles. Duke-Elder[7] has shown a rise of 26 mm. Hg in the ocular pressure of the dog following contraction of the orbicularis oculi muscle produced by electrical stimulation of the facial nerve.

This explanation does not fully account for the pressure variations observed in the present work for several reasons:

1. The ocular tension in the two eyes of the same individual using uniocular lid retraction showed no differences.

2. If mechanical factors were significant,

TABLE 3

VARIATIONS OF OCULAR TENSION IN GROUP III

(Measurements of ocular tension in curarized patients given 0.5% eserine into the conjunctival sacs (q 10 minutes ×5) followed by administration of electroshock therapy.)

	Eyes: Odd = right eye, Even = left eye	Ocular Tension after 1% Eserine q 10×5	Ocular Tension * After I.V. Curare	Shock Stimulus	Minutes																								
					1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	25	30	35	40	45	60
SCHIØTZ	1	17	18			44*					8		6						13						14		18			
	2	20	20			44*					9		6						15						17		19			
	3	35	31					44	33					10									21	27	27				
	4	27	26			44*	38	32		27		27				20			16			14		16	20				
	5	27	26			44*	36	32		27		27				23			17			14		20	20				
	6	25	24			44			23		20		17		14		15	14		15			17		17	17				
	7	23	22			44			23		17		14		10		12	14		15			14		17	17				
	8	20	20			44*		40		26		20		13	10			12		12				13	15		17			
	9	20	20			44*		37		25		17		11	9			11		12				12	15		18			
	10	23	20			44*		35		12			6		4			8					8		12	12			12	
	11	23	20			44*		35		12			6		4			8					8		12	12			12	
	12	24	22			44*	44*	40		21		17	10		8	7		10						14		16		19		
	13	24	23			44*	44*	40		20		15	9		7	6		10						14		17		17		

* Rise of ocular tension above 44 mm. Hg, i.e. beyond zero mark on Schiøtz scale.

the marked rise in ocular tension after electroshock in the curarized patients should be followed by a drop in pressure coincident with fluid displacement. Curare reduced but did not abolish the marked lid contractions so that if the mechanical theory was correct, the ocular tension should drop secondarily due to the expression of fluid from the globe.

3. The relatively slow return of the tension to normal suggests that factors other than simple mechanical displacement are important.

According to the tonometer data of Moses and Bruno,[8] a fall in ocular tension from 20 mm. to 8.0 mm. Hg would indicate a loss of about 12.8 cu. mm. of fluid from the eye. According to Grant,[9] the rate of aqueous formation is found to average 2.4 cu. mm. per minute. Therefore, the amount of fluid lost in patients following electroshock could be replaced within approximately five minutes, whereas 20 to 70 or more minutes were required. This presupposes that the rate of outflow at the angle in the hypotonic state was minimal or absent.

The suggestion that larger amounts of fluid leave the anterior chamber by diffusion than by flow may have significance in relation to the present work. Kinsey[1] states that "of the total movement of water out of the anterior chamber (50 microliters per minute) 2.75 microliters a minute leaves by flow and 47.25 microliters a minute leaves by diffusion."

One[1,2] of the controlling factors in fluid exchange may be the osmotic pressure differences between the aqueous humor and the plasma, the hypertonicity of the former being chiefly contributed by bicarbonate and ascorbate. Thus, variations in ocular tension

may be produced by osmotic pressure changes between the aqueous humor and blood and by changes in the rate of outflow at the angle.

The decrease in ocular pressure observed following electroshock may be induced by osmolar and permeability factors developing with the associated convulsion. The effect of electroshock upon cellular and extracellular fluid osmolarity has been studied by Welt and others.[5]

The electroshock convulsion was shown to be accompanied by a rapid redistribution of water manifested by a contraction of the extracellular fluid space and a rise of serum sodium concentration. These changes varied with the intensity of the convulsion and were reduced following curarization.

Altschule and Tillotson[10] demonstrated a decrease in plasma volume with hemoconcentration and increased plasma protein concentration following electroshock. These alterations may have resulted from the rise in cellular osmotic pressure associated with the convulsion.

Convulsive activity produces cellular hyperosmolarity by increasing the concentration of osmotically active particles within the cell.[5] Increased permeability of the cell membrane may be an added factor through the action of acetycholine liberated during the period of stimulation. In relation to the eye, the increased osmolarity of cellular and tissue fluids may exert an attraction to remove the aqueous until an equilibrium was established. This fluid, attracted into the interstitial area, would be carried into the capillaries and removed into the circulation. Readjustment of these fluid and electrolyte exchanges occurs upon cessation of the convulsion.

During recovery, the intracellular osmolar concentration decreases due to refabrication of larger molecular constituents and to changes in energy relationships which restore normal fluid and electrolyte distribution. In the eye, the restitution of the normal osmotic relationship would effect the gradual return of normal ocular tension as cellular hyperosmolarity, with the attendant influence on extracellular fluid osmolarity, decreased.

The rise in ocular tension observed in electroshock following curarization may be explained by the blocking action of curare upon acetylcholine. Acetylcholine appears to be an important factor in regulating membrane permeability, cell surface activity, and electrolyte transmigrations.[11] The inhibition of these effects by curare would tend to prevent or retard fluid and electrolyte exchanges thus preventing the fall in ocular tension observed in the noncurarized patients.

The elimination of vigorous muscle activity by curarization may also be a factor in preventing osmotic pressure differences between the fluid compartments. Thus, the ocular tension rise with curare may represent the resultant of the lack of diffusion of fluid from the aqueous due to acetylcholine-blocking together with the mechanical effect of contraction of the extraocular muscles.

A drop in ocular tension, following the initial rise seen with curare, was observed in the eserinized eyes. The presence of eserine by inhibiting cholinesterase permits the accumulation of acetylcholine locally so that a concentration sufficient to supersede the blocking action of curare develops. This effect is noted within 10 minutes when the decrease in ocular tension becomes manifest after the initial rise. The preservation of acetylcholine in this group will increase permeability, permitting fluid shifts to occur as a result of osmotic pressure differences.

It is postulated on the basis of the observations reported here that the recognized changes in the osmolarity of body fluids following electroshock may influence the blood-aqueous barrier. Increases in osmolarity induced by electroshock may cause diffusion of fluid from the aqueous, the rate of which may be influenced by several factors including the intensity of the shock and the concentration of acetylcholine locally. The im-

portance of acetylcholine in abetting these fluid shifts requires considerable further study. One practical example of the importance of this substance may be the finding of a parasympathomimetic substance in the aqueous of nonglaucomatous eyes and its complete absence in eyes with chronic simple glaucoma as reported by Bloomfield.[12]

To date we have had the opportunity to study the effect of electroshock on the ocular tension of only one glaucomatous patient. An ocular tension which varied between 40 and 50 mm. Hg was reduced, 30 minutes after the shock stimulus, to 19 mm. Hg and remained in a normal range for one and a half hours before steadily returning to preshock levels.

Investigations on the details of the mechanisms postulated to explain the present observations have been undertaken.

Summary

Following an electroshock stimulus, a fall in ocular tension was observed in 34 eyes. Unilateral lid retraction in 10 patients did not affect the decrease in tension noted in both eyes. The decrease in tension was maximal in four to five minutes with return to preshock levels occurring within 12 to 70 or more minutes.

The administration of curare prior to electroshock resulted in a marked rise in ocular tension during the convulsive phase. The tension fell rapidly to the preshock level and remained there.

Eserine placed in the eyes of curarized patients resulted in a drop in ocular tension after the initial rise had transpired.

Electroshock produces alterations in the cellular and extracellular fluid osmolarity which, in the eye, may affect the osmotic gradient to attract fluid from the globe. This may produce a transient decrease in ocular tension as the fluid enters the capillaries and is carried into the circulation. The possibility that acetylcholine is of some significance in furthering these shifts is suggested.

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METASTATIC TUMORS OF THE UVEAL TRACT*

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Numerous articles on metastatic tumors of the uvea have been written during the past four decades. The first report, mentioned frequently in the literature, was made by Perls[1] from autopsy findings in 1872. Since that time about 275 cases have been reported for an average of three and one-half cases per year.

This undoubtedly represents only a fraction of the cases actually occurring, since in generalized carcinomatosis the uveal metastases occur rather late. Likewise, visual symptoms of sufficient importance to lead to the clinical diagnosis are rarely found. Similarly, few routine post-mortem examinations include the eyes and the pathologic diagnosis is thereby missed. The frequency of individual case reports in the literature 15 to 20 years ago also probably discouraged reluctant authors from reporting a single case.

NATURE OF THE TUMORS

Metastatic tumors of the uvea are predominantly carcinomas; however, hypernephroma,[2] malignant melanoma,[3] sarcoma,[4] chorionepithelioma,[5] and teratoma[6] have all been reported.

Site of the primary tumor. The female breast is the site of about 65 percent of the primary tumors according to Cordes.[7] Others report from 60 to 72 percent from the same site. Lungs and bronchi account for 10 to 15 percent according to Giri[8] and Ask.[9] The gastro-intestinal tract is reported to contribute seven to 10 percent of the primary sites. Prostate, thyroid, adrenal, bone, skin, testicle, male breast, liver, parotid, ovary, and uterus have also all been reported as a location of primary tumors.

Site of the secondary tumor. Predominant location of the metastasis is near the posterior pole. Involvement of the anterior segment is said by Cordes[7] to be rare. Sanders[10] reported the ratio of choroidal involvement to iris involvement as about nine to one. Iris was reported by Reese[11] to be about seven times as commonly involved as the ciliary body. Cordes[7] states that only two cases have been reported where the ciliary body alone was involved. Optic-nerve involvement is infrequently mentioned in the literature.

Most authors agree that the incidence of bilateral metastasis is about 25 percent,[7, 12–14] although the involvement is seldom simultaneous. Ginsberg[14] states that the left eye is more frequently the site of metastatic lesions than the right.

Frequency of metastasis. Metastasis to the uvea is rare. Godtfredsen[15] in 1944 in a clinical study of 8,712 patients with carcinoma found only six with metastasis of the choroid. Goodsitt[16] stated that in one series of 100,000 admissions to an ophthalmic hospital there was only one metastatic tumor to the eyeball.

Mechanics of metastasis. Most authors agree that tumor cells are transported from the primary site through the blood stream to the eye. They are lodged in the small ocular vessels and finally break through the vessel walls into the surrounding tissues according to Cohen.[12] Many observers have demonstrated such emboli which implant themselves almost invariably in the uvea, while infectious emboli implant themselves in the retina in more than 90 percent of the cases.

Reese[11] speculates that the explanation of this is probably connected with the size of the emboli which determines their position in the blood stream. Bacterial or viral emboli, even if present in agglutinated masses, are much smaller than one neoplastic cell or one red blood cell and, therefore, would occupy the central and faster flowing portion of the blood stream.

As a result of this they would be carried

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to the end arteries and implant themselves. The tumor cells would course along the peripheral portion of the blood stream and would have a tendency to flow into the smaller tributaries, thus reaching the ciliary system and the uvea.

Duke-Elder[17] explains a predilection for the metastasis to involve the posterior pole by stating that the emboli would natually course through the 20-odd short posterior ciliary arteries rather than the two long posterior or the five or more anterior arteries.

The more frequent involvement of the left eye is explained by Parsons[18] as the same reason that the left cerebral embolism is more frequent; that is, there is a more direct pathway via the left carotid which comes off the aorta than the right which comes off the innominate.

Time of appearance of metastasis. The metastases may be found weeks to many years after the primary lesion is manifest, or they may be found before the primary lesion is discovered, as shown by Reese[19] in his report of four such cases. Venco[20] described a patient with a thyroid carcinoma who had metastasis to the choroid 14 years later. Von Sallmann's[21] patient had a 10-year interval between the appearance of the carcinoma of the rectum and its choroidal metastasis.

History. The loss of a portion of the visual field or actual loss of visual acuity found in choroidal metastatic lesions may be insidious in onset or may be sudden due to a detachment of the retina, or more rarely to hemorrhage into the optic nerve.

A history of tumors elsewhere in the body may be elicited or the patient may have symptoms referable to an undiscovered tumor. There may have been a history of a benign lesion or surgery for unknown causes.

It may be difficult to obtain history of malignancy. Women are sometimes reluctant to tell of the removal of their cervix, uterus, or breast.

The visual symptoms are usually unilateral; however, Cordes[7] states that bilateral involvement always suggests metastatic carcinoma, particularly in the presence of carcinomatous history. Pain in or about the eye may be a presenting symptom. Proptosis and/or chemosis may be found late in the disease.

Clinical findings. Early, a flat, solid appearing lesion is seen in the posterior pole. Cordes[7] states there may be one or more and that they are well-outlined, round, pale-gray, pale-yellow, or yellowish-gray, flat foci over which retinal vessels pass with a slight bend. The tumor, or tumors, increase rapidly in size. Hemorrhages may occur . They may appear mottled and usually cause an early detachment of the retina. Reese[11] states that necrosis of the tumor may give an inflammatory reaction, particularly when the anterior uvea is involved.

The progress of the tumor is rapid and detachment usually soon becomes complete. This rapid progression is helpful in differential diagnosis from other choroidal or retinal tumors. Although this is a space occupying tumor, significant rise in intraocular pressure is not necessarily a predominant finding. In fact the tension may be normal or lower than normal.

Pathologic findings. The type of tumor varies according to the primary source. Reese[23] states that a typical flat diffuse lesion is characteristic and to be expected because of the nature of the epithelium. He further states that this type is particularly common in metastasis from the breast. When the primary lesion is in the gastro-intestinal tract, liver, or thyroid gland, the lesion may grow either in a rather localized, elevated, or diffuse fashion.

The microscopic picture, according to Duke-Elder,[22] is dependent on the primary site, but individual tumors vary considerably. When the tumor is secondary to a breast carcinoma it consists of alveoli of various sizes containing large polygonal cells with single large nuclei. The stroma may be scanty or it may be abundant. The choroidal tissue is

ordinarily compressed and degenerated, and the chromatophores are distintegrated with a dumping of pigment. If a tumor is derived from the lung, liver, or gastro-intestinal tract it is adenocarcinomatous in structure.

Bock[24] reported an interesting metastasis from the liver that appeared green, contained tubules which were filled with green fluid, later proven to be biliverdin.

Prognosis. The prognosis is extremely bad. Usher[25] gave an average life expectancy of eight months, with a maximum of two years, after the metastatic lesion was found. Frequently, a patient may be moribund when first seen by the ophthalmologist. Evans[26] reported a patient with bilateral metastasis who lived two years and four months after the metastatic lesions were found. The moribund patients usually have metastasis to multiple organs, including the brain.

Treatment. Treatment to preserve life seems to be of no avail; however, Cordes,[7] Wilmer,[27] Reese,[28] and others have successfully preserved vision by using X-ray or radium therapy. Reese[28] recommends the same method with X rays that he uses for the treatment of retinoblastoma, excepting that the total dosage is reduced to 2,000 or 3,000 r.

Report of a case

A 59-year-old white woman, D. E., in March, 1950, visited the Letterman General Hospital Eye Clinic complaining of a loss of part of the left temporal field of vision for four or five weeks. She complained of some pain and lacrimation in that eye for a corresponding period of time. Past history revealed a hysterectomy 13 years previously for a malignancy of the cervix, with no recurrence. A history was also obtained of a chronic progressive cough for 18 months, with occasional blood streaked sputum. Bronchoscopy and examination of a coughed up specimen had revealed the presence of a nonmalignant adenoma of the left upper bronchus.

Examination of the eyes revealed a visual acuity correctible in both eyes to 20/20. The left fundus revealed a solid appearing detachment of the retina, elevated four diopters and located five disc diameters nasally to the optic nerve. The detachment was about two disc diameters in size.

The elevated retina was dark gray in color. It was bullous but not tremulous. Transillumination appeared to be normal. The tension was: O.D., 22 mm. Hg (Schiøtz); O.S., 14 mm. Hg. The external appearance of the eyes was normal as was the fundus of the right.

Immediate hospitalization was advised but the patient refused. She returned to her home, 100 miles away, with pinhole glasses and the promise to return in one week. At the end of three weeks, she returned with an interval history of having had pneumonia, which was treated with antibiotics. She had become nauseated and started vomiting and was acutely ill on admission to the hospital on March 7, 1950. Her civilian doctor had blamed the nausea and vomiting on the antibiotic therapy.

In this three weeks, the detachment had progressed to about twice the previous size, even though the patient had spent most of her time in bed. The patient's condition became steadily worse.

One week after admission the detachment had increased. It appeared yellowish-gray and solid. A bullous detachment had appeared inferiorly which was tremulous. On March 24th, two weeks after admission, detachment was complete.

Gradual proptosis developed during May and the patient died three months and 10 days following admission. At that time the eye was proptosed several millimeters. There was chemosis of the bulbar conjunctiva and scleritis apparent nasally.

Pathologic report

Autopsy demonstrated a primary adenocarcinoma of the left main bronchus, with

Fig. 1 (Maxwell). Tumor of orbit and choroid, showing defect in sclera which is apparently the area of break-through.

extension into the left upper lobe of the lung and metastasis to left regional lymph nodes, liver, right kidney, adrenal glands, brain, right sixth rib, and left eye.

Dr. Michael J. Hogan of the Proctor Laboratory, University of California Hospital, examined both eyes and the significant findings are herewith reported with his kind permission.

Gross examination. The right eye measured 24 by 24 by 25 mm. and was grossly normal. The left eye measured 26 by 25 by 24 mm. The cornea was hazy and appeared small. The anterior chamber was deep. The pupil measured five mm.

There was a tumor mass on the nasal side of the optic disc which had apparently grown through the sclera (fig. 1). The tumor measured about 18 mm. anteroposteriorly and 15 mm. vertically. It was elevated seven mm., was dense, white, and firm.

Horizontal calottes were made. There was a tumor which occupied the entire choroid in a flat fashion. It also involved the ciliary body (fig. 2).

Microscopic examination. The right eye was uninvolved with the tumor. The left eye had findings as follows:

CIRCUMCORNEAL TISSUES. There was a rather marked inflammation of the conjunctiva and episcleral tissues with edema, degeneration, and desquamation of the epithelium.

CORNEA. The cornea showed some edema of the basal epithelium and infiltration of the superficial stroma by round cells.

LIMBUS. Schlemm's canal was patent and the trabecular meshwork contained a few scattered inflammatory exudates and some edema fluid.

SCLERA. There was a rather marked scleritis throughout with invasion by tumor cells which will be described later. The vessels were congested and surrounded by inflammatory cells. This was particularly marked on the nasal side.

ANTERIOR CHAMBER. The angle was open

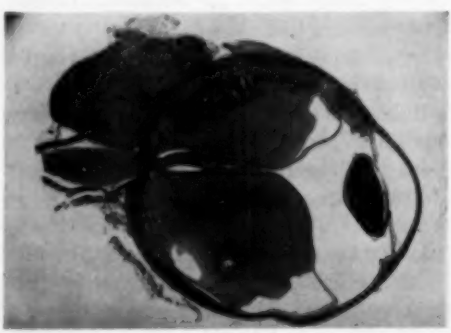

Fig. 2 (Maxwell). Involvement of the orbit, choroid, and ciliary body is demonstrated in this picture.

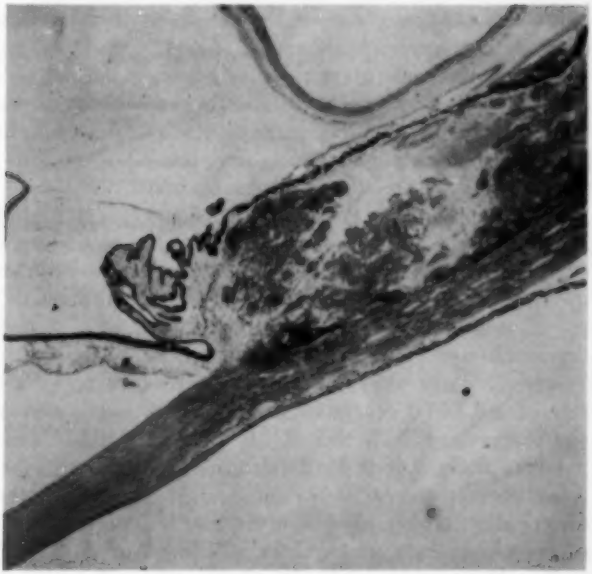

Fig. 3 (Maxwell). Showing involvement of the ciliary body.

excepting for a very narrow synechia. There was some clotted exudate anteriorly.

IRIS. The iris stroma showed moderate congestion and round cell infiltration.

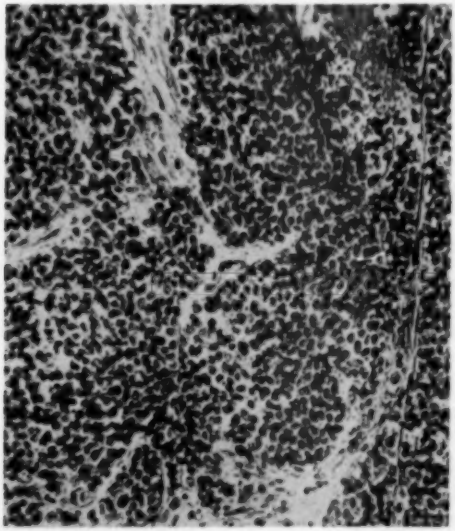

Fig. 4 (Maxwell). Showing tumor growing in islands and columns separated by connective-tissue matrix.

CILIARY BODY. The nasal portion of the ciliary body was extensively invaded by the tumor and partially detached. The tumor occupied mainly the muscular portion and suprachoroidea. There had been considerable hemorrhage from the tumor with detachment of the pars plana and almost the entire nasal choroid.

CHOROID. There had been metastases of the pulmonary tumor to the choroid on both the nasal and temporal sides of the optic disc. The tumor had extended forward into the ciliary body (fig. 3). Considerable hemorrhage had occurred into this tumor with resulting necrosis.

The growth extended out through the scleral fibers into the adjacent Tenon's capsule and also through the posterior emissaria into the orbital tissues. Small seedings were seen on the temporal side adjacent to the long posterior ciliary artery.

The optic nerve anterior to the lamina cribrosa had also been invaded and a portion of the peripheral retina on the temporal side adjacent to the disc was involved.

The tumor grew in columns and islands of

cells which were sharply separated from each other by connective tissue matrix (fig. 4). The individual cells grew as solid masses without intervening connective tissue; in general, the cells were rather large and anaplastic. Numerous mitotic figures were present. The nuclei were almost all rounded and contained prominent nucleoli. Occasional neoplastic giant cells were seen.

RETINA. There was a total separation of the retina by the developing neoplasm. The retina showed rather marked atrophy and degeneration except in the peripheral portion. Posteriorly there was congestion of the vessels, edema, and degeneration of the nuclear and supporting cells.

OPTIC NERVE. Except for the changes mentioned above, the nerve itself showed no gross abnormality. It may have been the invasion of the nerve which produced the initial field defect. However, it is more probable that hemorrhage into the tumor with detachment of the retina caused it.

VITREOUS. The vitreous was liquefied and detached to the anterior globe but showed no gross abnormality.

LENS. The lens was intact. The capsule had its normal contour. The epithelium showed no change. The cortex and nucleus showed some post-mortem degeneration but otherwise they were normal.

SUMMARY

1. A brief review of the literature of metastatic tumors of the uveal tract with a summary of the conclusions by various authors is presented.

2. A case is reported of a woman, aged 59 years, with previously undiagnosed adenocarcinoma of the bronchus, who had unilateral metastasis to the left choroid, ciliary body, and optic nerve, with extension through the sclera into Tenon's capsule, and also through the posterior emissaria into the orbital tissues.

3. The patient died four months after diagnosis and five and one-half months after history of the metastatic lesion.

4. The pathologic findings as concerns the involved eye are presented in detail.

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METASTATIC CARCINOMA OF THE CHOROID

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REVIEW OF LITERATURE

Metastatic carcinoma of the choroid is not common. Ask[1] collected 211 cases from the literature, 152 of which were verified by pathologic examination; in 59, the diagnosis was made clinically.

Only two cases of metastatic carcinoma of the choroid were recorded by Payne[2] among 70,000 eye patients at the New York Eye and Ear Infirmary.

Stallard[3] reported six cases from the Moorfield Hospital, a ratio 1:147,000. Godtfredsen[4] investigated 8,712 patients at the Radium Center and Eye Clinic of the Finsen Institute in Copenhagen. A systematic ophthalmoscopic examination was done between 1938 and 1944, on all cancer patients with eye complaints. Only six cases with metastatic carcinoma were observed. Two cases were from 1,287 patients with mammary carcinoma, two from primary carcinoma of the lungs, one from chorionepithelioma of the testicle, one from buccal carcinoma. Stallard gives the frequency of metastatic carcinoma of the choroid in Denmark as 1.5 per 1,000.

Kulvin[5] reported a case of metastatic carcinoma of the left choroid from a chorionepithelioma of the left testicle. He states that his case was the fifth reported in the literature and that all occurred in males under 30 years of age.

Greear[6] states that approximately 300 cases of metastatic carcinoma of the eye have been reported to date.

Spaeth,[7] in his recent review of ocular tumors from the Wills Eye Hospital and University of Pennsylvania Hospital, reports that only nine cases of metastatic adenocarcinoma were observed during the last 10 years among a large number of eye patients in the two institutions.

At the New York Eye and Far Infirmary pathologic laboratory, out of 4,000 enucleated eyes, only 15 cases of metastatic carcinoma of the choroid were encountered during the last 35 years (Kara[8]), which indicates the infrequency of the incidence of carcinoma of the choroid.

The rarity of metastasis to the eye is believed to be due to the fact that the ophthalmic artery branches from the internal carotid almost at a right angle, so that the cancer cells in the blood stream are carried past the narrow opening of the ophthalmic artery and

are deposited in the brain instead of in the uvea.

It is very likely that many cases of choroidal carcinoma are overlooked. The patient is too ill from general metastases to complain about impairment of vision and dies before an ophthalmoscopic examination is done. There is good reason to expect an increase in the number of cases of metastatic carcinoma of the choroid because of the use of intensive irradiation therapy which prolongs the patient's life.

Primary tumor site

The most common source of carcinoma of the choroid is carcinoma of the female breast. Cohen[9] gave the incidence as 70 percent, Usher[10] as 72 percent, Asbury and Vail[11] as 60 percent, and Pillat[12] reported that, of 200 cases of metastatic carcinoma of the choroid, 65 percent occurred from carcinoma of the female breast. He also described a case of metastasis to the choroid from a male breast, the fourth case reported in the literature.

Godtfredsen,[4] however, expressed his opinion that carcinoma of the lungs gives rise to metastasis in the choroid nearly as frequently as cancer of the breast; this, he believes, is due to better diagnosis of tumors of the lungs. He, therefore, pleads that a systematic ophthalmoscopic examination be made on patients with tumors of the lungs. If metastases are found in the choroid, the patient should not be subjected to the pulmonary operation.

The next in frequency as primary foci are the intestines, including the rectum, the prostate, thyroid, ovary, uterus, liver, kidney, and, in rare occasions, the testicle. Von Sallmann's[13] case seemed to be the first observation of a typical metastatic gelatinous cancer in the choroid from carcinoma of the rectum. François and others[14] reported a very interesting case in which the primary source was the adrenals. An alveolar type of carcinoma of the choroid was found in a male, aged 56 years, without apparent signs of disease elsewhere in the body. Four months later the patient died and on autopsy a bilateral carcinoma of the adrenal cortex was found. The authors stated that only one other case of metastasis to the choroid from an adrenal tumor had previously been reported.

Reese[15] reported four cases in which the metastasis in the eye was manifest before the primary tumor. In one case, a man, there was iridocyclitis with hypopyon and secondary glaucoma. On enucleation a metastatic carcinoma of the ciliary body was found. The patient died four months later of carcinoma of the lung. The second, a woman, had metastatic carcinoma of the choroid. A thorough medical examination showed no abnormality except a slight enlargement of the thyroid gland. The patient died a year later of adenocarcinoma of the thyroid gland. The third, a man, had metastatic carcinoma of the choroid and, on autopsy, carcinoma of the stomach was discovered. In the last patient no primary focus of cancer was found.

Reese[15] states that the frequency of mammary carcinoma as the primary source of uveal carcinoma is due to the fact that carcinomatous cells of the breast are most rugged of all cancer cells and are able to survive and propagate in surrounding tissues unfavorable to other cancer cells.

Choroid carcinoma

Choroidal carcinoma occurs bilaterally in about 25 percent of the cases. Usually both eyes are not affected simultaneously, but one following the other. Cohen,[9] Lemoine and McLeod,[16] Cordes,[17] and Zentmayer[18] have reported bilateral carcinoma of the choroid. Usher[10] states that in one third of the cases, metastatic carcinoma of the choroid occurs in both eyes.

Bedell[19] followed, with colored and black and white photographs of the fundi, the development of bilateral carcinoma of the choroid from the onset to detachment of the retina and secondary glaucoma. He believes

that the patient should not be subjected to enucleation of the eye (unless it is painful) as it does not stop metastasis to other parts of the body.

Usually the site of the first invasion of the choroid is in the vicinity of the posterior pole of the eye, on the temporal side near the macula, where the ciliary arteries are most numerous and large. The loose, highly vascular tissue of the choroid is an ideal nutritional medium for neoplastic growth. Ask,[1] however, does not believe in a special affinity of the uveal tissue for cancer metastases.

McDannald and Payne[20] and Greear[6] each reported a case of metastatic involvement first of the optic nerve, with subsequent extension to the choroid.

Duke-Elder[21] explains the preference for the posterior region of the choroid by remarking that emboli travel through the short posterior ciliary arteries more readily than through the long posterior or anterior ciliary arteries.

Interval of metastasis

The length of time between the diagnosis of the primary tumor and appearance of the metastatic tumor in the eye varies between several months and years, the average period being about two years. Stallard[3] reported the longest interval of metastasis to the choroid as 17 years after removal of the breast. In von Sallmann's[18] case, there was a lapse of 10 years between the discovery of the primary tumor in the rectum and the development of ocular metastasis.

The tumor spreads from the primary source to the metastatic area by way of the blood stream. The cancer cells form emboli (Cohen[9]) in the ocular vessels, then break through the vessel wall into the surrounding tissue. If there are no pulmonary metastases, then, in some cases, metastasis may occur at any point along the vertebral system. Jaensch[22] emphasizes that, before doing a radical mastectomy, the fundi should be examined. If metastasis is present in the eye, neither the breast nor the eye should be touched as the metastases are general and death will ensue in a few months.

Differential diagnosis

The differential diagnosis between carcinoma and malignant pigmented melanoma is very important.

Malignant melanoma is a primary neoplasm of the choroid which endangers the patient's life if the eye is not enucleated as soon as the diagnosis is made.

Metastatic carcinoma grows fast, the tumor is flat, usually spreads laterally, with little tendency to increase in thickness; the margins are not sharply defined; the color is grayish-pink or yellow. There is early loss of vision with development of a shallow detachment of the retina; glaucoma sets in late, though pain in the eye arises early. There is a history of a primary carcinoma elsewhere in the body.

In pigmented malignant melanoma the growth is circumscribed and projects forward, the color is dark, glaucoma sets in early, and the detachment of the retina is extensive. Often a shadow is present on transillumination.

The prognosis is invariably grave, as metastasis to the eye indicates generalized metastases and the patient usually dies within a few months to about two years after the ocular lesion has been noted.

Treatment

The treatment is palliative. Enucleation is performed if pain and secondary glaucoma set in. If the second eye is involved, then, in order to preserve some vision for the patient's remaining few months of life, irradiation therapy should be resorted to. These patients frequently are not aware of the hopelessness of their condition, but are concerned about losing vision in the remaining eye.

Zentmayer[19] treated successfully a case of bilateral choroidal carcinoma with radium.

Reese[15] recommends X-ray therapy in these cases. The special cones which he employs in the treatment of retinoblastomas afford accurate direction of the beam and eliminate scattering. He recommends a total dosage from 2,000 to 3,000 r. In one of his patients the vision was improved from 20/200 to 20/30.

In Lemoine and McLeod's[16] patient, 17 roentgen treatments improved the vision of the remaining second eye to 20/70. (The patient had lens opacities before X-ray therapy was given which accounted for the poor vision.)

Cordes[17] believes that X-ray therapy is the treatment of choice; it can be given by any well-qualified roentgenologist. He reported a case of a woman, aged 31 years, who had bilateral metastasis to the choroid, the primary focus being scirrhous carcinoma of the breast. One eye was enucleated and X-ray therapy was employed in the second eye. The patient was given 3,152 r initially and, 14 months later at the time of the recurrence of the process, an additional 3,562 r were given. The patient lived eight months after the recurrence and retained vision of 20/20 up to the time of her death. No opacification of the lens was seen, which indicates the tolerance of the eye to this type of irradiation.

Ellis and Scheie[23] recently reported two cases of carcinoma of the breast with metastasis to the choroid which were treated by sterilization.

One patient, aged 34 years, had a radical mastectomy two years before the appearance of a lesion in the choroid of the left eye. The enucleated eye showed metastatic carcinoma of the choroid; there were also a number of dense nodules in the lungs. Sterilization of the ovaries by roentgen rays was employed. The lesions in the lungs regressed and the patient lived two and a half years.

The second patient had bilateral metastatic carcinoma of the choroid, lesions in the lungs, skull, ribs, and pelvis. A sterilization roentgen dose was given to the ovaries. The ocular lesions and those of the lungs regressed and she lived eight months. The ovaries most likely stimulate the growth of the breast tissue during the menstrual cycle and sterilization may eliminate that factor and retard the course of the disease.

Case report

Mrs. A. P., aged 64 years, was referred to me for consultation by Dr. Anna Hubert on June 7, 1951. She gave the history of having noticed impairment of vision in the right eye for approximately eight weeks.

Examination. The vision in the right eye was reduced to finger counting at one foot on the temporal side. The lids, pupil, cornea, and iris appeared to be normal; the media were clear. The ocular motility was normal.

Ophthalmoscopic examination revealed the presence of an elevated area (about one diopter) in the choroid, on the temporal side, adjacent to the optic disc and extending about three disc diameters laterally, obscuring the details of the macula. The tumor was of an oval shape, yellowish-gray in color, with a smooth surface.

The borders of the optic disc were clearly outlined and the retinal vessels were normal. A small flat serous detachment of the retina was seen at the lower margin of the growth. The edges of the tumor were not sharply defined.

The field of vision was only a small superior temporal quadrant. The intraocular pressure was: R.E., 17 mm. Hg; L.E., 16 mm. Hg (Schiøtz). The left eye was normal in every respect and the vision was 20/20 with correction.

X-ray films of the skull showed no evidence of metastasis to the orbit; no bone destruction was seen. The optic foramina were within normal limits. There were no metastases to the ribs. A small nodule was observed in the right lower lung.

Past history. The patient was admitted to the New York Infirmary on April 30, 1946. One month previously she had noticed a lump with dimpling of the skin on the inner side

of the right breast. The admission diagnosis was: Carcinoma, right breast.

On May 2, 1946, a radical amputation of the right breast was performed by Dr. Anna Hubert. The findings at the operation were as follows: a small-sized mass located in the lower inner quadrant of the right breast; this was practically extended to the sternum and adherent to the sternum.

The pathologic diagnosis (Dr. Sophie Spitz) was: Infiltrating duct carcinoma, grade 2, metastases to several axillary lymph nodes (figs. 1 and 2).

The patient received X-ray therapy, 300 r daily, from May 14 until June 7, 1946, when she was discharged from the hospital. She received roentgen-ray' treatments subsequently, at certain intervals, during the five-year period of follow-up.

In view of the past history and the fundus lesion, a diagnosis of metastatic carcinoma to the choroid of the right eye from breast carcinoma was made.

The patient was admitted to the New York Eye and Ear Infirmary on July 11, 1951. The tumor had increased in size, the detachment of the retina was more extensive. The borders of the disc were indistinct. The vision in the right eye was only light perception on the temporal side. An enucleation of the right eye was performed on July 13, 1951. A gold ball was implanted in the socket. The patient was discharged from the hospital in 10 days with a well-healed socket.

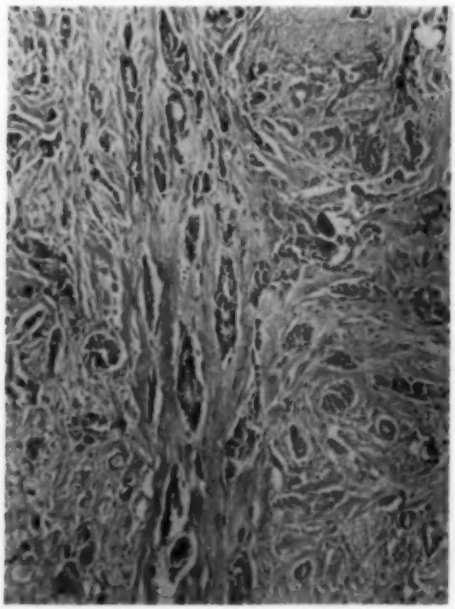

Fig. 1 (Sitchevska). Duct carcinoma of the breast (low magnification).

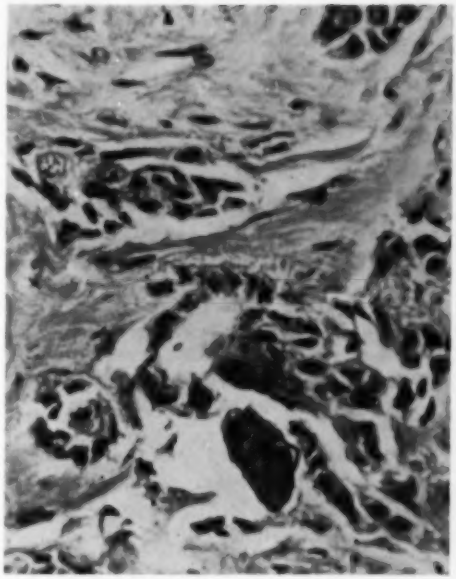

Fig. 2 (Sitchevska). Duct carcinoma of the breast. Calcific concretion with enclosed cells in one duct (high magnification).

Eye pathology report. The report (8396) from the Pathology Department of the New York Eye and Ear Infirmary by Dr. B. F. Payne follows (figs. 3, 4, and 5).

The globe is approximately normal in size and shape. It is characterized by a dark-staining mass in the choroid, adjacent to the optic nerve. The anterior chamber is shallow, the pupil is dilated, and the crystalline lens is prominent and large.

The sclera is relatively free of pathologic involvement except in the area immediately posterior to the tumor in the choroid. Here it is diffusely infiltrated with tumor cells.

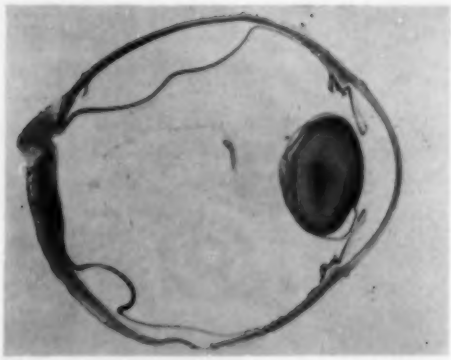

Fig. 3 (Sitchevska). Metastatic carcinoma of the choroid, circumpapillary.

The choroid shows no inflammatory change until the region of the tumor is reached. Only mild inflammatory reaction is present in the periphery of the tumor. Some of the sections show the mass partially surrounding the optic nerve. It is composed of epithelial elements arranged in glandular fashion with comparatively little supporting tissue. The tumor is flat and elevated about twice the thickness of the choroid.

The retina shows evidence of flat detachment on the nasal side. It is closely applied to the growth with atrophy of the rods and cones. About two disc diameters from the temporal margin of the tumor, the retina is undergoing various stages of degeneration. The retina shows cystic degeneration over the tumor and at the ora serrata on both sides. The rods and cones and other layers of the retina on the nasal side show degenerative changes which were undoubtedly caused by the detachment.

The optic nerve shows congestion and swelling of the disc with beginning invasion of carcinoma tissue.

The anterior chamber is shallow and partially filled with albuminous fluid. The iris angle is well rounded and the ligamentum pectinatum is in fair condition.

The crystalline lens shows evidence of nuclear sclerosis and thinning of the cortex. Posteriorly there are some fibers separated by fluid.

The vitreous is somewhat depressed and contains fibrin with intermingled cells. Considerable reaction is present in the region of the tumor.

Diagnosis. Metastatic carcinoma of the choroid with beginning invasion into the optic disc.

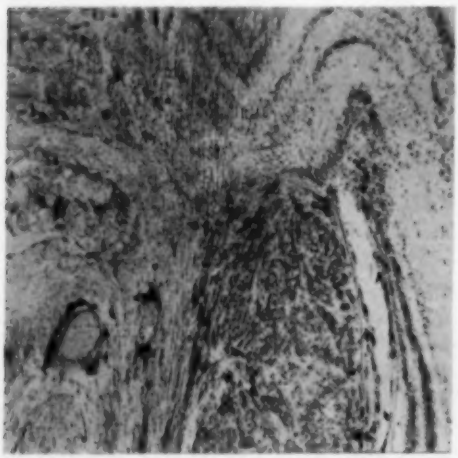

Fig. 4 (Sitchevska). Metastatic carcinoma of the choroid, showing invasion of disc margins (high magnification).

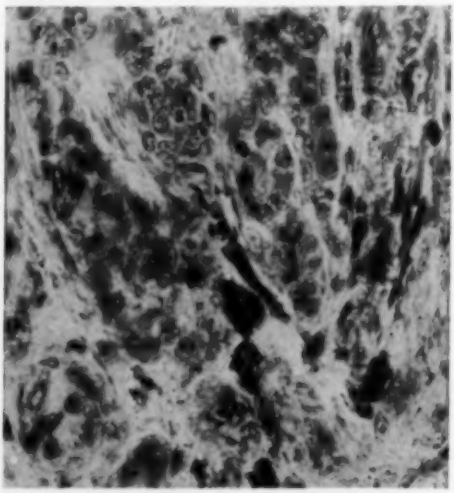

Fig. 5 (Sitchevska). Metastatic carcinoma of the choroid, showing ductlike arrangement of the tumor cells (high magnification).

The patient was last seen by me two months after the operation. No changes were seen in the left eye.

In October, 1951, she had a fracture of the neck of the right femur, so that she was unable to come for a check up from her distant home town. In February, 1952, she experienced severe headaches (which suggested intracranial involvement). Soon afterward, while bedridden, she broke her arm. She died on August 30, 1952—six years and four months after the radical mastectomy and 17 months after metastatis to the choroid of the right eye.

Conclusion

A case of metastatic carcinoma of the choroid from cancer of the mammary gland is reported. The clinical diagnosis was confirmed by the microscopic examination of the eyeball. The period between the appearance of the primary tumor and the metastasis to the choroid was five years and three months. Death occurred 15 months after the enucleation was performed. This interval justified enucleation, since the tumor was growing rapidly and might have caused secondary glaucoma, pain, as well as extraocular metastases.

I wish to emphasize that an ophthalmoscopic examination should be made in carcinoma of any organ in the body; undoubtedly, more cases of carcinoma of the choroid will thus be observed. Reports of each additional case of metastasis to the choroid will improve the statistical data.

The literature on metastatic carcinoma of the choroid is reviewed and brought up to date.

30 Fifth Avenue (11).

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FATE OF VISUAL FIELDS AND OPTIC DISCS IN PITUITARY TUMORS*

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During the decade of development of the transsphenoidal treatment of pituitary tumors by Hirsch[1] an enlarged sella by X-ray study was the most important diagnostic indication for surgical attack. On this basis in 59 patients, tumors were verified at operation.[1]

There were four additional patients, however, in whom the diagnosis proved to be disastrously incorrect despite conspicuous enlargement of the sella. Their visual signs were found to differ markedly from the predominant type of disc and field abnormality noted among 89 percent of the other 59 patients.

The attention of one of us (O. H.) became concentrated thereafter on the ophthalmic findings in all cases of suspected pituitary tumor; and during subsequent years patients presenting papilledema and atypical visual fields were accorded special scrutiny to rule out other conditions.

The earlier group of 59 patients (table 1) delineate more accurately than a later and larger group of 287 patients the possible varieties of visual field and optic-disc changes in the complex syndrome of pituitary tumor or parasellar tumor affecting pituitary and visual function. Pursuant to ophthalmic review[1] of the earlier cases, certain patients who presented papilledema and odd field defects were rejected for transsphenoidal operation. Subsequent progress in endocrinology and intracranial contrast study were helpful in a third group of 41 patients, operated on in collaboration with one of us (H. H.), when unusual clinical findings, such as papilledema and eccentric fields, led to pneumoencephalography which usually confirmed the diagnosis and disclosed the relative size of the tumor.

Pathologic analysis of the first group of 59 cases is as follows: 40 chromophobe adenomas, of which seven were cystic; 14 cases of acromegaly with eosinophilic tumors; two craniopharyngiomas; one chondroma; two cases in which the pathologic diagnosis was not determined. The pathologic findings in the subsequent 328 cases reflect the same general histologic distribution.

Unitemporal and bitemporal hemianopia, usually incomplete, was found in 84 percent (seven percent for colors only). Walker and Cushing[2] figured 31.7 percent for bitemporal hemianopia among 148 cases (1918) including 79 with unilateral blindness.

We list both uni- and bitemporal restrictions. Cases presenting temporal hemianopia in one eye—the other being normal or blind—cannot be used in determining the incidence of bitemporal hemianopia because the unitemporal defect may represent precursory or residual homonymous hemianopia. It was possible in most of our cases of this type

TABLE 1

VISUAL FIELD FINDINGS IN 59 CASES (1910–1919)

	Percent
Unitemporal or bitemporal hemianopia	84
Homonymous hemianopia	7
Unilateral nasal hemianopia	4.4
Central scotomas	11
Atypical fields	7
Primary atrophy	89
Papilledema	8.9
Postneuritic atrophy	4.4

* Read before the Section on Ophthalmology at the 101st annual session of the American Medical Association, Chicago, June, 1952.

—for instance, temporal hemianopia in one eye and blindness in the other—to ascertain from the history whether or not loss of vision started on the temporal side.

Homonymous hemianopia was present in seven percent (unilateral nasal hemianopia) 4.4 percent which may be regarded as an early homonymous hemianopia; altogether 11.4 percent.

Central scotomas (11 percent) were often erroneously considered to represent evidence of retrobulbar neuritis. Uncharacteristic fields were present in seven percent and were always associated with papilledema.

Pallor of the discs, classified as primary or simple optic atrophy, was observed in 89 percent. Loss of the whole temporal field was usually associated with optic atrophy; however, four patients had temporal hemianopia and diminished acuity with normal discs. On the other hand there were a few patients with pale discs and normal acuity. Papilledema was noted in 8.9 percent and postneuritic atrophy in 4.4 percent, altogether 13.3 percent as compared with 25 percent in an early series of unverified cases analyzed by Uhthoff[3] (1915) in which there were undoubtedly many errors in diagnosis.

Fig. 1 (Hirsch and Hamlin). Chromophobe tumor outlined by pneumoencephalogram (30 cc. air*).

* We have used this limited type of pneumoencephalography in 30 patients since 1946 with excellent diagnostic results and no complications.

TABLE 2

REVIEW OF CUSHING'S AND OLIVECRONA'S SERIES

	Percent
Cushing (1938) 260 chromophobe tumors	
Bitemporal hemianopia (lower quadrant defects excluded)	65
Homonymous hemianopia	10
Olivecrona (1950) 232 chromophobe tumors	
Bitemporal hemianopia	63
Homonymous hemianopia	3
Optic atrophy (bilateral)	51.4
(unilateral)	21
Normal discs (bilateral)	27.6

Papilledema or optic neuritis are signs that warn against the diagnosis of pituitary tumor. In such doubtful situations a limited type of encephalography (fig. 1) or even angiography should be used and will often help to settle the problem.

A review of Cushing's cases[4] (1938) and Olivecrona's series[5] (1950) shows approximately the same proportion of bitemporal hemianopia (table 2). Our incidence of 84 percent pertains to unitemporal and bitemporal hemianopia.

Our figure for atrophy shows approximately the same frequency—84 percent as compared with 72.4 percent of Olivecrona. The percentage of bilateral normal discs (Olivecrona)—27.5 percent—seems surprisingly high and suggests the likelihood of earlier diagnosis as the condition became more familiar.

Our figures for acidophil tumors are similar to those of other authors and demonstrate the currently well-known fact that about 50 percent of acromegalics are spared visual disturbance because they have small secretory tumors situated below the diaphragm and not encroaching on the optic chiasm.

Among the second group of 287 patients treated from 1920 to 1938, there are 58 on whom systematic ophthalmic observations

TABLE 3

SIX CASES WITH NORMAL DISCS*

Patients	Findings
2	Complete hemianopia
4	Incomplete hemianopia or temporal scotomas (These 6 patients with normal discs were operated on at different times: all of them showed postoperative widening of the fields and improvement of acuity of vision.)
3	Retained normal discs during available time of observation, i.e. 11 mo., 2 yr., 3 yr.
3	Showed pallor of the disc some time after successful operation. 1—3 weeks after operation 1—Retained normal discs for 3 yr. but temporal pallor developed after recurrence 1—With complete hemianopia regained after operation normal acuity and normal fields of vision. The discs remained normal for 8 years, turned pale after recurrence.

* Among 58 cases operated from 1920 to 1938 at the clinic of Prof. J. Meller, Vienna, by O. Hirsch. Follow-up study by F. Fischer.

were recorded by Fischer[6] for periods up to eight years.*

In Table 3 the findings of Fischer are summarized on six patients who had normal discs at initial examination. All of them showed improved vision after operation. Only two had complete bitemporal hemianopia; the other four had temporal scotomas or slight restrictions. There was no relationship between field defects and degree of visual acuity reduction.

During the follow-up period, three of the six patients continued to show normal discs up to three years after operation. One patient was observed for 11 months. The second was followed for two years and the third for three years—both maintaining normal discs although the latter developed transient return of bitemporal restriction which receded under radium therapy.

The other three patients developed postoperative changes in their normal preoperative discs; nevertheless, lasting improvement in visual function was accomplished by transsphenoidal decompression of the chiasm:

One patient showed prompt expansion of visual field and increased acuity but optic pallor was noted three weeks after operation which persisted for a 10-month follow-up period.

* Ophthalmology Clinic of Prof. J. Meller at the Allgemeinekrankenhaus in Vienna.

One patient showed normal discs for three years postoperatively when temporal pallor developed concomitant with recurrence of tumor.

One patient with normal preoperative discs despite bitemporal hemianopia and diminished acuity showed rapid restitution of fields and acuity following operation; eight years later the left disc became pale but improvement continued in this left eye which had exhibited greater loss of field and acuity than the right eye before operation. This individual was considered to have developed recurrent growth of a chromophobe adenoma which receded by radium application.

We attribute the delay in optic pallor to descending or retrograde atrophy which requires a lapse of time to become manifest in the disc. These data indicate that in the chiasmal syndrome from compression by pituitary tumor with normal discs, even after successful decompression, pallor may develop.

The most frequent change of the discs is temporal pallor. Of those 58 patients operated on at the clinic of J. Meller,[1,6] Vienna, 32 patients had temporal pallor. In 28 of these 32 patients, the improvement of acuity in vision and of the fields lasted for a number of years. In spite of this, the temporal pallor increased in some patients.

Among the 58 patients at Meller's clinic were 20 patients with total pallor of both sides. All had severe bilateral loss of acuity

and some had unilateral blindness. Visual fields showed complete loss of temporal half and restriction of nasal half also. There were 10 in whom the discs were recorded as showing equal degree of pallor over the nasal as well as the temporal side. In the other 10, the temporal part looked more intensely white; whereas, the paleness of the nasal part was tinged with pink and this color difference persisted throughout long periods of observation.

To explain the temporal pallor we bear in mind that the temporal part of the disc is normally lighter in color than the nasal part, the former being constituted of a thinner layer of nerve fibers and having a larger physiologic excavation. Diminished acuity of vision is caused by involvement of the papillomacular bundle which is located mostly in the temporal portion of the disc.

In cases in which visual acuity has been restored, the papillomacular bundle, although compressed at the chiasm, fortunately had been decompressed in time so that only axonal demyelinization progresses as the axis cylinders recover their function. The exact pathogenesis of the varieties of pallor may be attributed to decreased vascularization or even to diminished local requirement of blood flow or to secondary structural neuropathologic changes which can alter the refractile properties of the disc and produce the appearance of pallor on examination.

Gartner[7] recently described a case of chiasmal syndrome presenting a sharp bitemporal hemianopia and fair acuity of vision which was carefully followed during life to post mortem. Microscopic examination revealed a straight-line defect through the center of the macula with degeneration of the ganglion cells on the nasal side and their preservation on the temporal side. There was no sparing of the macula in the field studies nor on histologic examination so that visual acuity was maintained by the temporal half of the macula.

Conclusions

Normal optic discs are infrequent in pituitary (or parasellar) tumors that encroach on the chiasm but may be found occasionally even in patients with bitemporal hemianopia and diminished visual acuity. Decompression of the chiasm often restores acuity and field of vision but seldom prevents the delayed appearance of temporal pallor. We have never seen a pale disc restored to normal appearance after treatment; although such cases may have been observed by others. Damage to the chiasmal nerve fibers produces the inevitable sequel of retrograde or descending atrophy that eventually becomes visible in the disc.

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Discussion

Dr. Gilbert Horrax: My presence here as a neurosurgeon is due entirely to my Boston neighbors but, of course, I am very glad to say a few words in discussion of Dr. Hirsch's and Dr. Hamlin's paper, which they very kindly sent me to read.

Dr. Hamlin and Dr. Hirsch have referred to the difficulties which all of us had in the early days of pituitary surgery, about diagnosing the proper type of lesion in the undertaking of transsphenoidal operations, and I certainly would like to compliment Dr. Hirsch for being one of the pioneers in the development of the transsphenoidal operation, which served an excellent purpose in those days and still may to some extent, because he certainly was one of the very first to do this operation; it was later taken up by others, as you know.

There were difficulties of the type he has mentioned in the way of choked discs and other abnormal findings which made the diagnosis uncertain and the results uncertain in some of these patients.

Dr. Hirsch and Dr. Hamlin have made some important and interesting contributions to the various types of field defects which are present in pituitary lesions, showing the abundance of true bitemporal hemianopia. I think the discrepancy which they have shown between their 80-odd percent of true bitemporal defects and those of Henderson's review of Cushing's series, would not be so far apart if Henderson had taken into consideration the temporal hemianopia of one eye and the nearly blind field in the other eye as did Dr. Hamlin and Dr. Hirsch.

I have had occasion to look up about 40 of our patients in the Lahey Clinic and found that, if that observation was considered, that is, the temporal hemianopia of one eye and blindness in othe other, the trouble probably started as a temporal defect in that eye too. There were about 89 percent of the patients who probably had bitemporal hemianopia at one stage.

Dr. Hirsch has shown very well why there is so much greater defect in one eye than in the other eye because the tumor may grow against one optic nerve or the chiasm on one side; although the usual thing is, of course, for it to bulge up in the middle between the optic nerves.

There are other types of field defects with which I think we are all familiar—the rare homonymous type in which the tumor presses back against the optic tract back of the chiasm.

I have no figures for the amount of optic atrophy or the number with optic atrophy, but I think we have all seen patients who had a very marked optic-nerve pallor with fairly normal visual acuity, doubtless because of the sparing of the papulomacular bundle. Conversely, sometimes we see discs which look only slightly pale with a rather marked visual loss.

Also, Dr. Hamlin does well to speak of the fact that some of these patients with atypical defects, choked discs and so forth, need some further study to differentiate their lesion from other lesions around the chiasm. One of the principal lesions, and one which we have learned to do something about, is the occasional aneurysm which may give a large sella just as in pituitary adenoma. In the old days that sort of mistake must have been made.

I can remember years ago, even with a craniotomy, coming down on an aneurysm and just putting a needle in it and getting out pure blood. Of course in those days, one had to stop there and put some muscle over the aneurysm and close up. Now we do an arteriogram to demonstrate the aneurysm if there is any question about it, or an air study if that seems more practical.

You all saw Dr. Bedell's beautiful photographs showing how abnormal nerves can differ in their pallor and the extent of their pallor.

Just a word about the operation: The

transsphenoidal operation may and still does serve a useful purpose, particularly when the tumor largely extends down into the sphenoid cells, and perhaps the chiasm can be decompressed in that way.

Most neurosurgeons, I think, feel that they must do more than just decompress the chiasm in these lesions to get the best permanent end results. Dr. Hirsch had some very beautiful examples of long-term end results in the types of visual fields and acuity which he showed.

If one considers the five-year mortality, however, that is, the patients who have died within five years of tumor recurrence, in Dr. Cushing's series (which was done largely by the transsphenoidal method) the five-year recurrent mortality was 32 percent or a little over that. Dr. Hirsch's figures for that period were 19.8 percent, whereas, in patients with craniotomy (that we do) the five-year mortality is 8.6 percent.

The criticism of the craniotomy has been that it is a more risky operation than the transsphenoidal. That is true only when there are large intracranial extensions of the tumor. With the ordinary type of adenoma I decompress the chiasm by removing the tumor in the sella and the mortality is between two and three percent; for large intracranial tumors (really brain tumors), the mortality is much higher. The combined mortality for those two groups is somewhere between 13 and 14 percent.

One other thing I wish to bring out in regard to the treatment of these tumors, although it was not particularly the subject of this paper, is that the X-ray treatment of pituitary adenoma has become much more definite in recent years. With the ordinary type of X-ray machine the results were fairly good. With the two-million volt machine that is now being used at the Massachusetts Institute of Technology, to which I have access, results are better. In the last two years I have had exactly 35 patients who have been subjected to this treatment, 28 of whom have been sufficiently improved by the treatment not to require operation.

In some of the other cases I have operated and have found just an adenoma which was shrunken away. Why there was visual loss after that, I don't know. In one instance there was a completely empty sella.

I do think we ought to bear in mind that these tumors may be treated not only by surgery but also by X rays.

DR. H. HAMLIN: Our presentation deals with the ophthalmic findings in nearly 400 cases rather than the therapeutic merits of the transsphenoidal versus the transcranial operative approach. Dr. Hirsch[8] has published his results with the transsphenoidal method. The operative case mortality was, in the pre-antibiotic era, 5.4 percent, including craniopharyngiomas, in comparison with the operative mortality of 13.3 percent by the cranial method, excluding craniopharyngiomas which have an operative mortality of 40 percent. Since antibiotics, the operative mortality by the transsphenoidal method is two percent. In Hirsch's[8] publication can be found a comparison of long-lasting improvements by both methods. Of 140 improved patients, 73 percent showed lasting cures of five to 19 years after transsphenoidal operation in comparison with 54 percent of 130 patients operated by the cranial method[8] and followed for two to 18 years[8] (excluding craniopharyngiomas).

IRIS PIGMENT NODULES COMPLICATING MIOTIC THERAPY*

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It is the purpose of this report to call attention to an increased incidence and severity of pigmented nodules developing in the irises of patients who have received repeated instillations of potent miotic drugs.

Vogt seems to have been the first to call attention to nodules forming in the pigment epithelium at the pupillary margin in glaucoma patients who had received repeated administrations of pilocarpine and eserine.[1,2] He believed these nodules to be cysts rather than hyperplasia or edema of the pigment epithelium.

These "pilocarpine-eserine cysts" seemed transient and frequently were observed to disappear when miotics were discontinued. They developed in the pigment epithelium at the pupillary border or from the posterior surface of the iris but did not lead to adhesions between the iris and the lens nor to disturbances in vision.

It has been my experience and also that of Otto Barkan that pupillary pigment nodules of minor degree not uncommonly develop in patients who receive repeated instillations of pilocarpine;[3] however, I have not observed them to develop to a sufficient degree to disturb vision in patients receiving only this drug.

Since the advent of intensely acting miotics such as DFP (di-isopropyl fluorophosphate), carbachol (carcholin), and mintacol (di-ethyl-p-nitrophenyl phosphate), pigment nodules at the pupil not only have been seen much more frequently in the University of Oregon Medical School Eye Clinic but they also develop to larger sizes.

In addition to the more frequent formation of these nodules following use of the more potent miotics, there is other evidence that the violent contraction of the iris sphincter induced by these drugs probably pinches the epithelium against the lens with resultant fluid retention. No such nodules have been observed to develop in aphakic eyes. Furthermore, they seem much more frequent in children and young adults whose pupils react more intensely to miotics than those of older persons. Occasionally, these nodules have been observed in our patients above the sixth decade but they have been small.

It is not implied that intense miosis is the sole basis for development of pupillary margin cysts. They may occur after trauma or inflammation. Cowan has reported their occurrence on a familial basis and spontaneous development of these cysts was recorded as early as 1864.[4]

In most of the patients observed at the University of Oregon Medical School, it was not possible to tell by biomicroscopy whether the nodules were cysts or simply flocculi developing from hyperplasia or edema of the pigment epithelium. However, in some patients, a cystic character of the larger nodules was quite evident. One was observed to break loose and float freely in the aqueous.

As already noted, pigment nodules at the pupillary margin develop more frequently and to a larger size when strong miotics are prescribed than when pilocarpine alone is administered. Also, the stronger miotics make the pupil smaller and more readily subject to obstruction. I have observed six patients in whom iris nodules developed to such a degree that vision was obstructed when the pupil was contracted maximally.

In 1940, C. S. O'Brien and I observed a 35-year-old, one-eyed woman with a chronic noninflammatory type of glaucoma. Carbachol (carcholin) induced such an intense miosis that the pupil appeared almost pinpoint.

* From the Department of Ophthalmology, University of Oregon Medical School.

The ocular tension dropped to average levels, and uncorrected visual acuity was better than before she received the drug.

After about five weeks of using two instillations daily of 1.5 percent concentration of Carbachol, she noted a marked impairment of the vision to develop over a period of 48 hours. She was led into the clinic in a state of extreme agitation.

Examination revealed that several pigment nodules had developed and were obstructing the patient's tiny pupillary area. Vision returned as soon as the pupil was allowed to enlarge but then surgery was required to control the ocular tension. The pigment nodules disappeared within three months.

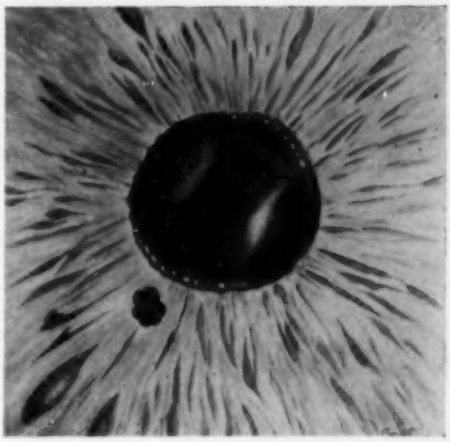

Fig. 1 (Swan). Cysts arising from the pigment layer of the iris.

Case reports

Since 1945, five patients have been observed who have had serious disturbances in vision due to obstruction of a miotic pupil by pigment cysts which developed following the administration of 0.1 percent DFP (diisopropyl fluorophosphate).

There were three children with glaucoma who were receiving daily instillations of 0.1 percent DFP in oil prior to or between operations.

In the first patient, a 13-months-old boy, ocular tension had been maintained at a normal level and the cornea had cleared with daily instillations of a 0.1 percent solution in oil. Four months later, the mother noted that there were periods, particularly during the first few hours after instillation of the drug, that the child seemed almost blind. Examination revealed multiple pigment cysts which completely obstructed the pupil when miosis was maximal. It was possible to reduce the dosage and still keep the tension controlled. Vision was restored but progress studies were not possible because the family left the community.

The other two patients were children of preschool age who had multiple operations in infancy for glaucoma but whose ocular tension was not adequately controlled without daily instillations of 0.1 percent DFP. Both of these children over a period of months developed, first, pigmentary nodules and, then, cysts which obstructed vision to the extent that the youngsters were unable to get about. Further surgery became necessary in these two older children and the cysts gradually subsided but small pigment nodules remained.

Two young adults also developed visual disturbances following prolonged administration of 0.1 percent DFP.

One was a man, aged 24 years, who had a rise in ocular tension and a serious loss of visual field associated with marked degeneration of the pigment epithelium of his irises. Initial examination revealed that his aqueous contained many floaters and that the chamber angles were filled with pigment. There were heavy melanin deposits in the iris stroma and on the back surface of the corneas.

Ocular tension could not be controlled with pilocarpine but was brought down to 18 to 20 mm. Hg (Schiøtz) with two instillations daily of a 0.1-percent solution. There was no further loss of visual fields and as long as the pupillary reflex was eliminated by the

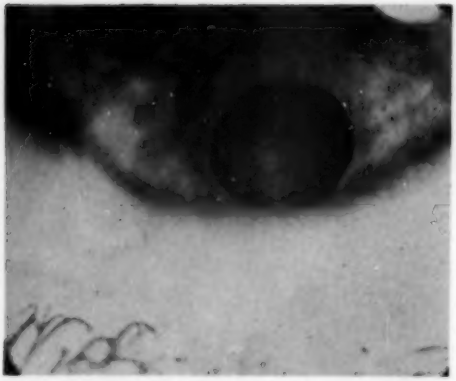

Fig. 2 (Swan). Cyst lying free in the inferior part of the anterior chamber.

complete contraction of the sphincter, the aqueous was free of floating pigment.

Six months later, the patient noted decreased visual acuity in one eye which was most pronounced one to six hours after instillations of the drug. Pigment nodules had formed at the pupillary margin of both eyes, but in the left, there were two large cysts which completely obstructed vision when the pupil was contracted. A third cyst had broken free, ruptured and was resting on the iris stroma (fig. 1).

Fortunately, the largest of the two pupillary cysts disappeared between examinations, apparently rupturing. The patient noted a recovery in vision even though his medication was continued. Since then he has continued on the same dosage of DFP for more than a year. From time to time, small cysts have formed at the pupillary margins and disappeared.

A second young adult was a woman with chronic glaucoma who complained that, following instillations of DFP, she had a persistent disturbance in vision. Her medication had been prescribed elsewhere so that it was not possible to determine the status of her irises before medication was begun.

Examination revealed a rounded brown pupillary cyst at the pupillary margin of one eye. This cyst had the features of others developing after miotic drugs but was considerably larger being about two mm. in diameter. It was possible to discontinue miotic therapy in this young woman but the cyst continued to enlarge and, after about six months, it broke free from the iris and lodged in the inferior part of the anterior chamber (fig. 2).

Clinical investigation

In recent months Mintacol (di-ethyl-P-nitrophenyl phosphate), an anticholinesterase compound developed in Europe, has been investigated in the clinics at the University of Oregon Medical School.[5] Instillations of minute amounts of the drug into the conjunctival sac promptly induce an intense miosis and cyclotonia lasting many hours. Its ocular effects are comparable to those of DFP. Mintacol can be prescribed for glaucoma patients in an aqueous solution but is less stable than DFP.

In one young adult who required instillations of an 0.012-percent solution every 12 hours, pigmentary nodules were noted after four weeks developing at the pupillary margin. These have not disturbed vision and treatment is being continued. Further studies will be necessary to determine the frequency with which nodules develop with this potent and promising new drug.

In none of the patients just reported did the pupillary pigment nodules produce a permanent disturbance in vision. This complication, therefore, should not be considered a contraindication to the prolonged use of potent miotic drugs in children and young adults; however, ophthalmologists should be aware that it occurs and should be prepared to alter treatment if it becomes apparent that the patient is going to develop an alarming disturbance in vision due to pupillary obstruction.

Summary

In 1920 Vogt described cysts developing in the pigment epithelium of the iris at the

pupillary margin in patients receiving pilocarpine and eserine. These nodules were transitory and did not disturb vision.

In phakic patients receiving more powerful miotics like Carbachol (carcholin), DFP (di-isopropylfluorophosphate), and Mintacol (di-ethyl-P-nitrophenyl phosphate) I have observed these pigment nodules to develop with considerable frequency and reach considerable size.

In three children and four young adults the nodules developed to such a degree that vision was obstructed when the pupil was extremely miotic. The loss of vision was not permanent but caused great alarm to the patients and their families. For this reason, ophthalmologists should be aware of this consequence of prolonged therapy of glaucoma with powerful miotic drugs.

3181 S. W. Sam Jackson Park Road (1).

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PERIPHERAL IRIDECTOMY

Technique, mechanism and the cause of hemorrhage

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The vicious circle in narrow-angle (iris-block) glaucoma consists of increased seclusion of the pupil, or "congestive glaucoma," bombé of the iris, narrowing and closure of the angle.[1-3] Initial shallowness of the axial depth of the anterior chamber is a frequent predisposing and causal factor.[12] A secondary anterior displacement of the lens occurs during the course of this type of glaucoma. It aggravates the seclusion and is an integral part of the vicious circle.[4,5]

Iridectomy equalizes the pressures in anterior and posterior chambers. By so doing it widens the angle, prevents peripheral adhesions, and exposes the trabeculum to aqueous. This is associated in many cases with retroplacement of the lens as shown by the increase in the axial depth of the anterior chamber.[1-5] Thus, iridectomy reverses the vicious cycle in narrow-angle glaucoma.

In early cases the action of iridectomy is complete provided the incision is sealed. It normalizes the pressure in those cases in which the trabeculum is not obstructed by adhesions or its permeability has not been reduced by previous contacts with the iris.

In the present article two techniques of peripheral iridectomy are reviewed. They were employed in a series of 100 cases. In the beginning of the series, before the ab externo technique with a sealed incision was developed to a satisfactory point, iridectomy was performed through a valvelike self-sealing corneal incision combined with a deepening of the anterior chamber.[1,2] Later in the series an ab externo technique was used which consisted of a sclerocorneal scratch incision, very small where it enters the anterior chamber and sealed with a prelaid suture.[6] This technique differs slightly from the one described by Chandler.[6] The action and effectiveness of peripheral iridectomy has recently been confirmed by Haas and Scheie.[11]

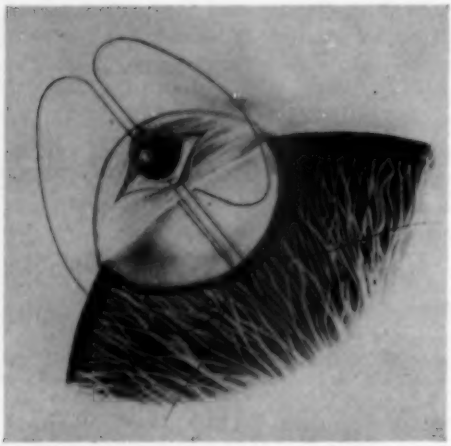


Fig. 1 (Otto Barkan). A scleroconjunctival suture is prelaid and a scratch incision made 1.0 to 1.5 mm. long where it enters the anterior chamber. The root of the iris plugs the wound, is prolapsed and excised. The anterior chamber is retained.

The ab externo technique, in its present form, is preferred because of its simplicity and safety.

The results of both techniques, with sealed incision, were used for the analysis of the specific action of iridectomy.

Peripheral iridectomy ab externo performed with a sealed incision

The usual preliminary measures are used, including a superior rectus suture. The pupil should be miotic. Pontocaine local anesthesia, no retrobulbar injection, is given.

The essential features of the ab externo technique are: the conjunctiva is raised with an injection of zylocaine. The conjunctiva and Tenon's capsule are incised six mm. above the limbus. The flap is reflected over the cornea. A vertical scratch incision 1.5 to 1.75 mm. posterior to the corneoscleral border in the 11- or 1-o'clock meridian is made. The superficial incision of the sclera, made with either keratome or Bard Parker knife, should be five mm. long to give ample visibility.

When the incision has penetrated about one-half the thickness of the sclera a 6-0 double-armed black silk suture is prelaid and is continued through the base of the conjunctival flap. An assistant stretches the scleral sutures thus exposing the deeper layers. Hemorrhage should be stopped with cautery and the area kept dry for perfect visibility. The size of the inner scratch incision where it enters the chamber (the last layers of transparent corneal tissue) should be as small as possible, not larger than 1.0 to 1.5 mm. It can be exactly controlled by scratching with the tip of a keratome.

If the incision where it enters the chamber is sufficiently posterior and not more than 1.0 to 1.5 mm. long the fluid in the posterior chamber will consistently cause the iris to plug the wound before aqueous can escape from the anterior chamber (fig. 1). If the iris does not prolapse so that it can be grasped it can be made to do so by the assistant slightly stretching apart the wound margins. The prolapse is grasped at its base and the tension on the sutures is released. The root of the iris is stretched to either side before cutting (in two cuts) with a small Barraquer iris scissors, in order that when the iris snaps back, the coloboma may extend beyond the inner wound, thus discouraging adhesions and assuring basality. This manner of making the sclerocorneal incision and the excision of the iris avoids the need of having to enter the chamber with an instrument and retains the chamber during and after completion of the iridectomy.

Two peripheral iridectomies are prone to be more effective than one, but usually one suffices.[1]

An interesting observation was the immediate postoperative deepening of the peripheral portion of the anterior chamber which was first described by Curran.[12]

A tremulousness of the iris diaphragm was also observed when the cornea was tapped with a glass rod. The impression of a postoperative slack iris diaphragm was encouraged by the observation of a localized bulg-

ing which persisted in some cases over an area of four mm. in diameter. Its position could be changed by pressure on the cornea. The pupil maintained a miosis of 1.5 mm.

Peripheral iridectomy through a self-sealing valvelike corneal incision

This technique is described because early in the series it helped to analyze the action of iridectomy. Clinically it has been superseded by the ab externo technique.

The pupil should be miotic. If the pressure is increased and the chamber is markedly shallow, it is advantageous to do a posterior sclerotomy. In order to facilitate the making of the beveled keratome incision a preliminary deepening of the anterior chamber is made through a prelaid valvelike puncture[1, 7, 8] (fig. 2). If the posterior sclerotomy is not followed by escape of fluid or if a malignant course is anticipated, 0.2 cc. of vitreous is aspirated from the posterior portion of the vitreous compartment with a #18 needle through a prelaid puncture at the pars plana as has been previously suggested.[1, 2]

The incision with the keratome begins at the corneoscleral border (fig. 3). The direction of the blade is first at a 45-degree angle but almost immediately (before the tip enters the chamber) the handle is depressed so that the blade lies parallel to the iris or points slightly toward the vertex producing a two mm. bevel. The incision is almost entirely intracorneal (figs. 2 and 3).

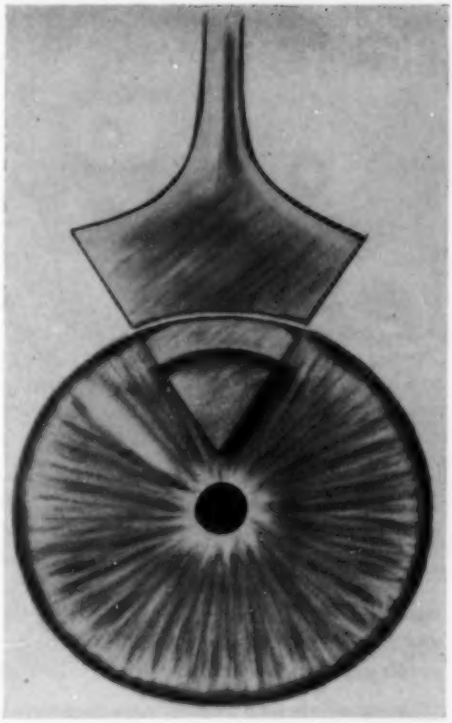


Fig. 3 (Otto Barkan). Keratome incision (valve or self-sealing).

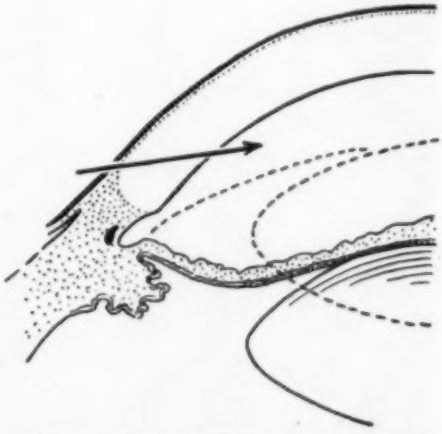


Fig. 2 (Otto Barkan). Deepening of the anterior chamber through an oblique, self-sealing puncture. Arrow indicates plane of incision creating corneal shelf. Dotted line shows position of iris and lens previous to deepening.

The surgeon faces the patient's right shoulder. The closed blades of the angulated knurled forceps* are inserted with the handle held vertically between the fingers of the left

* Made by the Storz Instrument Company, Saint Louis, Missouri. The shanks are bent at a right angle two mm. from the tip. From the elbow to the tip the blades do not come into contact in order to prevent the possibility of grasping the iris except at the tip. The teeth are placed at right angles on the opposing surfaces of the blades to avoid picking up iris while the closed end of the forceps glides over the iris.

Fig. 4 (Otto Barkan). Forceps is inserted and kept in plane of iris. It is then moved to end of incision in this plane. Dotted line indicates position of corneal shelf.

hand so that the tips point toward the palm of the hand (fig. 4). The closed tips are moved to the end of the incision (fig. 5) and are carried around the shelf by rolling the handle between fingers and thumb in a clockwise direction (fig. 6). After contacting the angle wall the forceps is tilted toward the patient's forehead to pick up a fold of the root

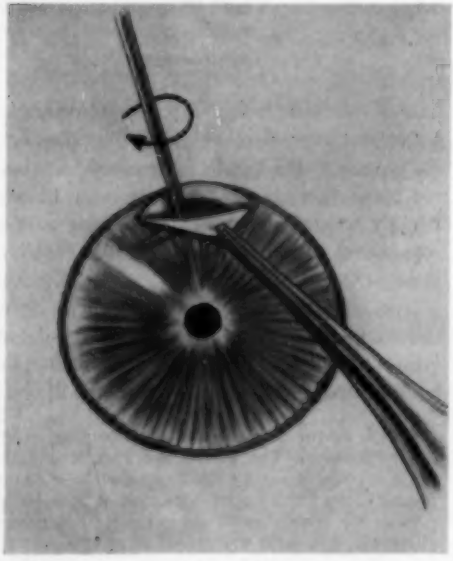


Fig. 5 (Otto Barkan). Insertion of forceps: Corneal flap retracted to show shelf. At end of incision forceps is rotated in order to carry blade behind the corneal shelf.

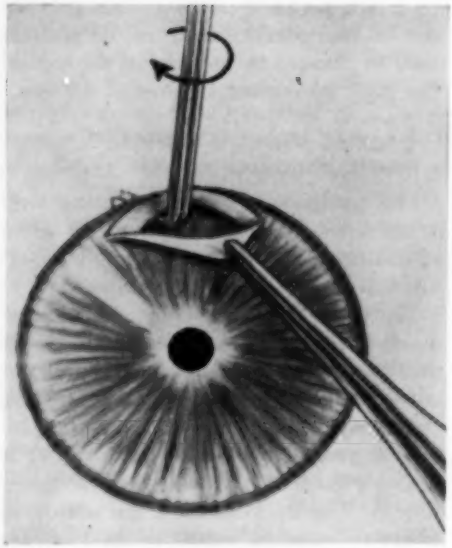


Fig. 6 (Otto Barkan). Corneal flap retracted to show position of forceps behind the corneal shelf.

of the iris. The iris is withdrawn to the temporal side and cut with small Barraquer scissors from the nasal side (fig. 7) and then withdrawn to the nasal side while the

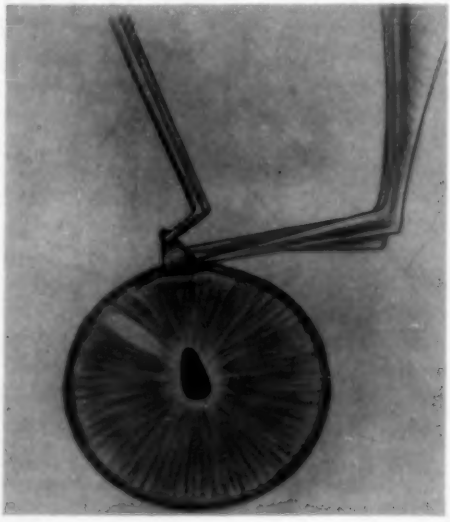


Fig. 7 (Otto Barkan). The handle is tipped slightly, the root of the iris grasped, pulled out, and the first cut is made.

temporal portion is cut (fig. 8). The central tongue is then drawn out and cut (fig. 9). On the left eye the temporal side is cut first. The surgeon's position at the side of the patient permits him to observe the pupil at all times. The anterior chamber becomes re-established within a matter of minutes since the aqueous cannot escape through the trap-door or valve incision. The patient should leave the operating room with the chamber reformed. If the chamber does not reform spontaneously physiologic saline solution is injected through the prelaid puncture.

The inner lip of the beveled incision is three to four mm. from the angle. The iris is cut while stretched around this corneal shelf. As a result, the cut iris retracts from the incision and adhesion of pillars does not occur (fig. 10). That the root of the iris may be consistently excised in the presence of a wide corneal shelf is proved by postoperative gonioscopy. The iris was cut off from the ciliary body without leaving more than a trace of a stump (fig. 14).

The disadvantages of the technique are that the forceps enters the chamber, that it is more difficult than the ab externo technique, and that it requires, in most cases, a preliminary deepening of the anterior chamber. It is, therefore, no longer used.

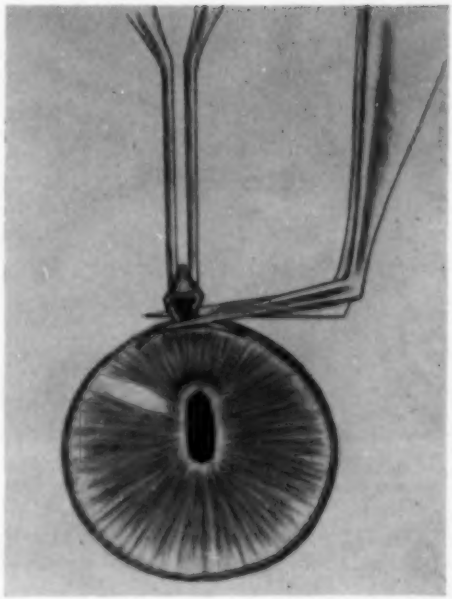


Fig. 9 (Otto Barkan). Third cut.

Analysis of iridectomy performed with a wide corneal shelf

The results of this technique were useful for a study of the mechanism of iridectomy.

It seems surprising in view of the fact that the incision where it enters the anterior

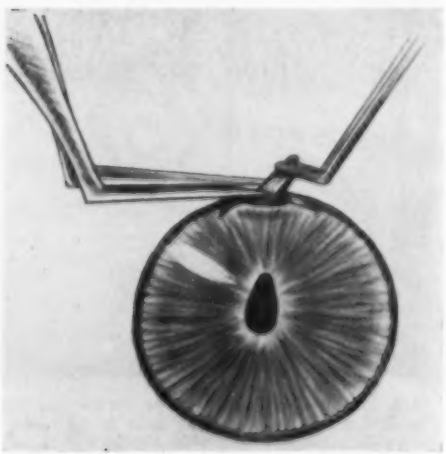


Fig. 8 (Otto Barkan). Second cut.

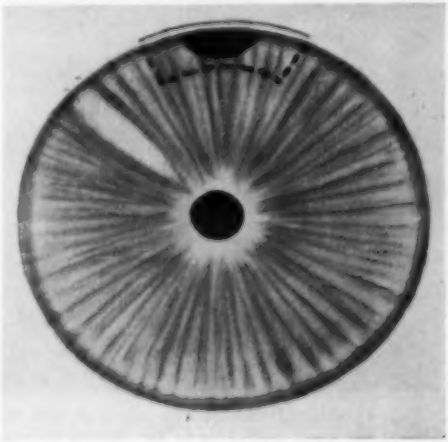


Fig. 10 (Otto Barkan). Coloboma. Dotted line indicates position of corneal shelf.

Figs. 11, 12, and 13 (Otto Barkan). Experiment demonstrating the mechanism of iridectomy when performed around a corneal shelf.

(A) Sheet of plastic representing the corneal shelf.

(B) Elastic band representing a radial segment of iris.

(C) Represents anterior surface of the ciliary body.

(D) Represents insertion of the iris to the anterior surface of the ciliary body.

Fig. 11 (Otto Barkan). The iris is grasped with forceps one-half inch from the insertion to the anterior surface of the ciliary body.

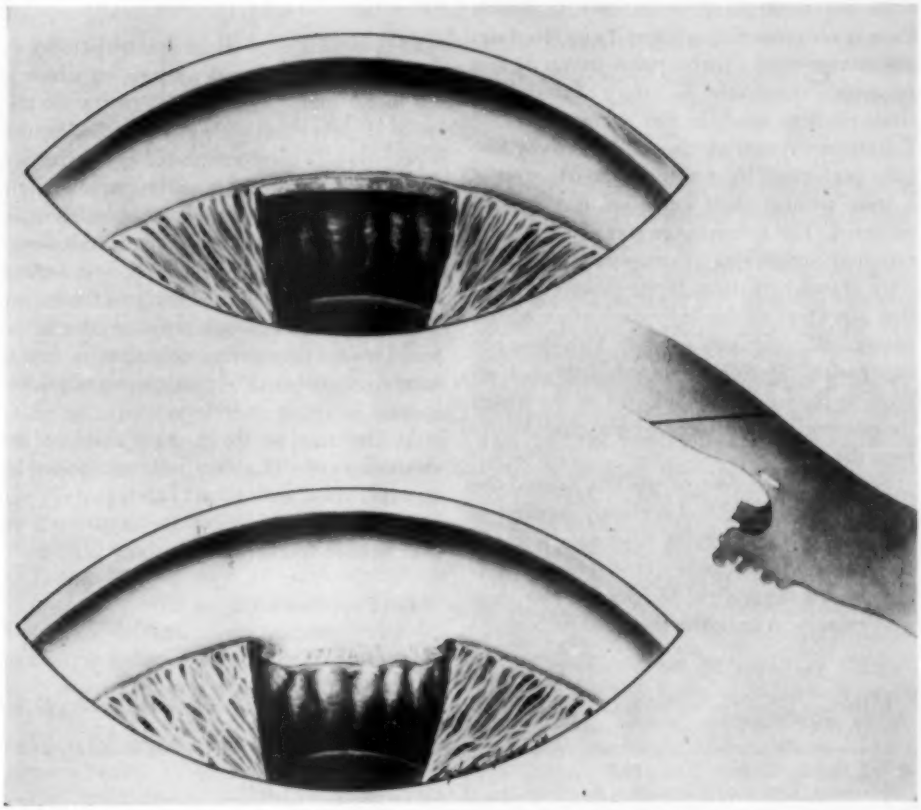
chamber is situated three to four mm. anterior to the root of the iris, that the iridectomy performed was always basal. The paradox can be explained by the following experiment (figs. 11, 12, and 13).

The distance between the incision where it enters the chamber and the root of the iris (that is, the corneal shelf) is represented by a sheet of plastic three-inches wide (A). An elastic rubber band (B) represents a radial segment of the iris, one end of which is attached to the plastic by means of a clamp. The attached end represents the anterior surface of the ciliary body (C). D indicates the insertion of the iris to the anterior surface of the ciliary body. If the band is grasped with forceps one-half inch from the insertion of the iris (D), drawn out around the edge of the plastic (which corresponds to the inner wound lip of the corneal incision), and there cut off with scissors (fig. 12), it will be found that, due to having been stretched, it has been cut very close to or at the prelaid mark which represents the root of the iris (fig. 13).

This experiment shows that a corneal incision placed some distance from the root of the iris, far from discouraging basality of

Fig. 12 (Otto Barkan). The iris is drawn out around the inner wound lip of the corneal incision and cut off.

Fig. 13 (Otto Barkan). Because the iris has been stretched, it has been cut very close to the root of the iris.



Figs. 14 and 15 (Otto Barkan). Gonioscopic views following peripheral iridectomy.

Fig. 14 (top). Postoperative gonioscopic view following peripheral iridectomy made around a wide corneal shelf. The root of the iris is excised almost flush to the ciliary body. A trace of stump remains.

Fig. 15 (bottom). Postoperative gonioscopic view following peripheral iridectomy made around a wide corneal shelf with resulting marked hemorrhage. The anterior surface of the ciliary body has been sheared off.

Inset shows position of corneal shelf and represents in cross section the area of the tissue excised.

the excision, actually encourages it provided the iris is grasped sufficiently near its root and that it has normal elasticity. It also shows the rationale of some stretching of the iris in any kind of iridectomy.

Basality of the coloboma is also the objective of Parker's intracorneal incision for iridectomy.[9] The incision is made oblique with a Graefe knife but in the opposite to the usual direction. However, according to Goldmann,[10] who employed it to study the "pure" action of iridectomy, it involves considerable hazards.

The Cause of Hemorrhage Following Iridectomy

Hemorrhage following iridectomy has, in the past, usually been considered to be the result of vascular disease or congestion. In my experience this explanation is inadequate except in cases of obvious abnormal vascularity or dyscrasia.

In the usual basal iridectomy in which there is not more than a trace, if any bleeding, gonioscopy shows that a small stump of iris remains. Presumably, the artery of the major circle remains intact in this stump (fig. 15).

In three eyes on which total iridectomy had been performed by stretching the iris around a wide corneal shelf extensive hemorrhage occurred. The hemorrhage was evacuated by repeated irrigations. Postoperative gonioscopy showed in these three cases (fig. 15) that a portion of the anterior surface of the ciliary body had been excised. This does not occur with iridectomy performed through an incision placed close to the root of the iris in the conventional manner and grasping the iris near the sphincter.

Stretching the root of the iris around the broad corneal shelf had evidently resulted in inclusion of the artery of the major circle in the excision. This can be avoided by not pulling the iris beyond the incision farther than is necessary to complete the excision.

Conclusions

1. A technique of peripheral iridectomy ab externo performed with an incision which is 1.0 to 1.5 mm. long where it enters the anterior chamber and sealed by a prelaid suture is reviewed. It is recommended as an effective and safe operation in early narrow-angle glaucoma and as a prophylactic procedure.

2. A technique of peripheral iridectomy performed through a beveled self-sealing corneal incision was used early in the series. It is described. Although replaced later in the series by the ab externo technique its results were employed with advantage to analyze the specific action of iridectomy.

3. The role of the corneal shelf in the mechanism of iridectomy is demonstrated by an experiment with elastic bands.

4. An explanation for the occurrence of hemorrhage following iridectomy is given.

490 Post Street (2).

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POSTOPERATIVE ENDOPHTHALMITIS*

A CASE REPORT AND DISCUSSION OF CLINICAL ASPECTS AND TREATMENT

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In this paper, endophthalmitis will be considered to be an inflammation of the structures lining the vitreous cavity and panophthalmitis to be an inflammation which involves all of the structures of the eyeball.

In many cases, there may be a question in differential diagnosis between endophthalmitis and panophthalmitis. However, in considering an infection of the eye, the difference between endophthalmitis and panophthalmitis becomes one of degree of involvement of the eyeball.

CASE REPORT

The following case of endophthalmitis (from the service of Dr. William J. Harrison) is deemed worthy of reporting because it is a case of postoperative intraocular infection which recovered with retention of the eye.

H. F., a white man, aged 53 years, was admitted to the Wills Eye Hospital on January 8, 1952, for cataract extraction in the right eye although the vision in the left eye was 6/6.

Cataract extraction was considered because he showed a rubeosis of the right iris infratemporally and also a prominent episcleral vessel in the corresponding region. It was felt this might indicate a malignant melanoma. Transillumination was normal.

Vision of the right eye was hand movements and the cataract had a tense capsule with a dense nucleus, anterior subcortical vacuoles, and dense cuneiform opacities of the cortex.

Preoperative studies, including conjunctival cultures, dental examination, nose and throat examination, blood sugar, blood Wassermann, and urinalysis, were negative.

At operation, the capsule ruptured during delivery and the vitreous presented, a small bead being lost.

On the second postoperative day the patient complained of a sore throat. The throat looked normal on examination and the temperature was normal.

On the fifth day postoperative, a grayish membrane started to form in the pupillary area, and the posterior capsule and anterior vitreous seemed hazy. The patient was started immediately on 3.0 gm. of chloramphenicol orally and 1.0 gm. every four hours. Chloramphenicol was used because of its ability to penetrate into the intraocular fluids, as demonstrated by Leopold, Nichols, and Vogel.[1]

On the sixth postoperative day the eye, grossly, was the same. Examination under the slitlamp showed stromal haze of the cornea, aqueous flare, and the anterior chamber was filled with gossamerlike strands of dirty light-brown material. The vitreous was cloudy and the posterior capsule also showed a dirty light-brown coating.

When no improvement was shown on the seventh postoperative day, he was started on cortisone by mouth and cortisone locally.

The eye gradually became less red and the corneal lustre returned. When he left on the 20th postoperative day, the eye was only moderately red and he had a vision of hand movements at three feet. At this time he was well. He showed no blood effects clinically from the chloramphenicol.

DISCUSSION

Every case of postoperative endophthalmitis poses many puzzles. The first to be considered is whether the endophthalmitis is exogenous or endogenous.

* From the Wills Eye Hospital.

Exogenous or endogenous endophthalmitis

Since there is no reason to believe that this is a case of endogenous or metastatic endophthalmitis, one must suppose that it is due to an infection introduced externally at the time of surgery or at one of the dressings.

In any case of endophthalmitis, however, it is possible that the infection comes from within the body itself. That is why intraocular surgery is not done on patients with dental, nose and throat, genital, or any infections in the body. This is demonstrated by the following reports of two cases of endophthalmitis in which organisms were cultured from the intraocular fluids but in which there was no history of trauma or surgery.

The first case of metastic endophthalmitis without injury or surgery to the eye was reported by Nicholls and Locatcher-Khorazo.[2] Their patient was a 48-year-old woman who had a stabbing pain in the right eye. She had no injury and no operation.

The lids of the right eye were swollen and red, and the globe was under tension, the anterior chamber was shallow, and the pupillary area was obstructed by an opaque mass. The pupil did not react to light. Vision was limited to light perception. The temperature when first seen, two days after the onset, was 99.2°F.

Treatment was started with 200,000 units of penicillin in bees-wax, intramuscularly, and also four to five gm. of sulfadiazine by mouth each day. Diabetes was discovered and treated with insulin. There was no evidence of foci of infection. Evisceration finally was necessary. The organism identified was Escherichia coli communior.

The germ killed mice, but not a guinea pig and caused a fulminating panophthalmitis in rabbits' eyes when injected into the anterior chamber. However, when the cornea was inoculated by scarification with a needle which had been dipped into the culture or by instillation into the conjunctival sac, infection did not result. The organism in vitro was resistant to penicillin, but markedly sensitive to streptomycin.

This endophthalmitis was probably metastatic in origin. When one considers that, in many cases of postoperative endophthalmitis, the conjunctival smears and cultures are negative, it is easy to understand that endophthalmitis might be due to metastatic infection from a remote portion of the body attacking the tissue devitalized by surgery.

The second case, a baffling one, was reported by Houlton.[3] The patient, a 17-year-old youth, was seen because of an inflamed right eye which he said had previously had poor vision. He gave no history of injury. This right eye was proptosed and showed chemosis of the conjunctiva and swelling of the orbit. The pupil was dilated and inactive, the iris brown instead of blue. There was a plus tension of the eye, the cornea was hazy, and a slight hyperemia was present. The upper part of the anterior chamber contained a large mass.

The eye was treated with eserine drops and sulfathiazole tablets were given by mouth in a dosage of 30 gr. at once and 22.5 gr. every six hours thereafter. The eye was enucleated 25 days after the onset. There was no light perception at this time.

The pathologic examination revealed a necrotic mass with no cells seen and with a large amount of melanin pigment. The pathologist suggested this was probably a necrotic malignant melanoma but he could demonstrate no tumor cells.

The left eye became inflamed 10 days after enucleation of the right eye. Examination showed injection of the eye, some keratic precipitates on the cornea, and vascularization of the iris. Culture after a vitreous puncture showed Staphylococcus albus, diptheroids, and saprophytic organisms. The eye went on to vascularization of the cornea, ciliary staphyloma, and loss of light perception.

Houlton[3] considered this to be a case of

bilateral endophthalmitis. The course of events were certainly unusual and, in review, it must be considered, just as the author did, a case of metastatic endophthalmitis. It is conceivable, however, that these events could be preceded by surgery, or precipitated by aseptic surgery.

Antibiotic and chemotherapeutic agents

The question of which drugs to use in the case herein reported did not present a problem because chloramphenicol was known to have superior ability to penetrate the intraocular fluids. However, it is interesting to follow chronologically the methods of treating endophthalmitis.

Before the sulfonamides were discovered intravenous typhoid therapy was the treatment of choice. It is still of value, and perhaps should be used with the new chemotherapeutic agents and antibiotics which, although credited with saving eyes, are not panaceas for intraocular infections for a number of reasons. In order to be effective these agents must be: (1) Used early, (2) be specific, (3) be capable of penetrating the blood-aqueous barrier, (4) and be used in large doses.

Antibiotics are not as broad spectrum as could be desired. Specific organisms need specific chemotherapeutic agents or antibiotics, and there are certain organisms and strains of organisms against which nothing is of value. When an overwhelming infection occurs, cultures to identify organism and strain take too long.

It is well known that these agents do not readily penetrate the blood-aqueous barrier to enter the intraocular fluids. Until the advent of chloramphenicol, the sulfonamides were most effective in this respect, and reports of eyes saved by their use began to appear soon after their introduction.

In 1938, Harry[4] reported four cases of penetrating injury of the eye saved by sulfanilamide. Butler[5] reported a case of gonorrheal endophthalmitis, occurring on the 37th postoperative day in which he felt the eye was saved by sulfanilamide.

Experimental studies with sulfanilamide appeared this same year. Given systemically, it showed penetration into the eyes of rabbits,[6] dogs,[7] and human beings with abnormal eyes.[8,9]

In 1942, Scheie and Leopold[10] injected microcrystalline sulfathiazole intraperitoneally into cats and showed that this agent does not enter the eye in as great concentration as sulfanilamide, sulfapyridine, or sulfadiazine. However, in infected eyes much larger amounts enter into the aqueous and the vitreous.

In 1943, Leopold and Scheie[11] in studies with microcrystalline sulfathiazole showed significant penetration into the aqueous after subconjunctival injection of sulfathiazole in the usual or in the microcrystalline form. Both forms penetrated equally well. Penetration was aided by the use of histamine.

Robson and Telbrich[12] used topical sodium sulfacetimide on rabbits and felt it produced high levels in the cornea, conjunctiva, and anterior chamber of the eye. Von Sallmann[13] found that sodium sulfadiazine orally was of some use against pneumococci types III, VII, and X indicted as responsible for some cases of panophthalmitis. Meyer, Block, and Chamberlain[14] demonstrated that systemic sulfapyridine penetrates into the aqueous humor.

In 1945, Green and Jakobovitz[15] reported a case of endophthalmitis in an aphakic eye. A culture of nonhemolytic staphylococcus was obtained. This eye did not respond to intravenous sulfadiazine and oral sulfamerazine but the authors felt it cleared up two days after intramuscular penicillin was started. This is one of the few cases in which penicillin seemed to help intraocular infection more than sulfonamides.

It has been shown repeatedly that systemically administered penicillin does not penetrate readily into the vitreous humor.[16–19] In

inflamed eyes, penetration increases. If it reaches the vitreous, however, penicillin does have some effect on vitreal infections according to a number of authors.[16-20]

Rycroft,[21] however, preferred sulfonamides to penicillin. (This was before the days of streptomycin, aureomycin, terramycin, and chloramphenicol.) In his hands intramuscular penicillin did not influence the course of deep infection of the eye. He tested eyes which had been enucleated following intramuscular penicillin injection. The ground-up media did not inhibit the growth of germs. He did not have success with intravitreal injection of penicillin.

Mann[22] used 1,000 units of intravitreous penicillin. It was impure and caused severe exudative choroiditis, cataracts, and optic atrophy. Her clinical feeling was that it helped a few eyes. Kelly[23] used intravitreous penicillin in nine cases with equivocal results but thought it better than no treatment at all.

Reports on streptomycin followed. Leopold and Nichols[24] demonstrated that systemic streptomycin penetrates poorly into the intraocular fluid. Bellows and Farmer[25] showed that, after 100 μg. of intravitreal streptomycin, a therapeutic concentration can be expected for over 24 hours.

Somerville-Large[26] reported a case of panophthalmitis, due to Bacillus proteus, which developed in a premature baby on the first day after delivery. Streptomycin was started and the eye looked better but perforation occurred. No germs were cultured from the eye after the streptomycin was started.

R. Shoemaker[27] reported a case of penetrating injuries to both eyes. Tetanus and gas gangrene toxin (U.S.P.) were given and 4,000 units of penicillin every three hours. In spite of penicillin therapy, the left eye had to be enucleated because of severe endophthalmitis. The right eye became more and more turbid and the anterior chamber was irrigated with 5,000 units of penicillin per cc. The culture showed gram-negative bacilli.

Four days after injury, streptomycin was given systemically (0.5 gm. every four hours) and 9,000 μg. were given intravitreally. The next day the eye was worse, and intravitreous streptomycin was repeated in a dosage of 1,400 μg. A streptomycin pack containing 20,000 μg. per cc. was placed in the cul-de-sac for one hour.

On the ninth day, vision was nil but on the 13th day, light perception returned and the inflammatory reaction began to subside. The patient also had intravenous typhoid vaccine. Later, a linear cataract extraction was performed and eventually vision was 16/200 to 20/200.

Later laboratory reports in Shoemaker's case showed the organism to be the gram-positive, spore-forming Bacillus brevis. Surprisingly, sensitivity tests showed the organism to be more susceptible to penicillin than to streptomycin.

The intraocular penetration of aureomycin and terramycin is low. Terramycin topically, subconjunctivally, and orally has been shown to penetrate poorly into the normal intraocular fluid and tissues of the normal rabbit.[28]

Luce[29] reported a case of endophthalmitis in which the eye recovered with useful vision. Oral terramycin was one of the drugs used. A. deRoetth, Jr.,[30] showed aureomycin did not penetrate into the intraocular fluid when given orally or intramuscularly, although high blood levels were present with both methods. No aureomycin was detected in the aqueous after corneal baths. These results, also appear to be true clinically. Bellows and Farmer[31,32] showed that bacitracin is generally effective against the same organisms susceptible to penicillin.

On the other hand, Leopold, Nichols, and Vogel[1] showed that chloramphenicol does penetrate into the intraocular fluids. When given intravenously in a concentration of 50 mg./kg. body weight, chloramphenicol penetrates into the anterior chamber rapidly. It also penetrates into the vitreous but in lower concentrations. Secondary aqueous humor

contained higher concentrations, indicating that more will penetrate into inflamed eyes. Chloramphenicol in drops or ointment will penetrate the cornea.

In a later article, Leopold[32] recommends the use of chloramphenicol clinically as prophylactic therapy and in the treatment of ocular infections.

It would seem that the possibility of blood changes is not a contraindication to the use of chloramphenicol because the drug can be so valuable and does not have to be used over too long a period of time. However, blood counts should be taken every two or three days and compared with the blood count before chloramphenicol therapy.

There is a constant search for therapeutic agents to use in intraocular infections,[34] as well as endless studies on the idiosyncrasies of the bacteria which produce them.[35,36]

Thus, what happens to an eye depends not only on the strain of an organism and the pathogenicity this strain has for the eye but also on the number of organisms introduced and the resistance this strain has developed against the particular chemotherapeutic agent or antibiotic used.

Since all these factors are almost impossible to evaluate in time to save the eye, a schedule of treatment should be followed as recommended by Leopold.[33] He reported five cases of intraocular infection after cataract extraction. Of five eyes, two were saved by oral chloramphenicol with visions of 6/15 and 6/20. One was saved by a combination of terramycin injected into the anterior chamber, and penicillin and streptomycin subconjunctivally.

Cortisone and intraocular infection

Mixed therapy was used in the case herein reported but the clinical course was not definitely changed until chloramphenicol was begun. Those of us who watched the case definitely felt the chloramphenicol was of value, and seemed to halt the infection. However, there was marked improvement following cortisone therapy. It is difficult to evaluate the effect of the cortisone or to say which agent helped the most; both seemed to help.

It has been shown by Cook and McDonald[37] that cortisone will reduce the increased permeability of the blood-aqueous barrier following ocular inflammation. On the other hand, McDonald, Leopold, Vogel, and Mulberger,[38] using streptomycin in severely inflamed eyes, could not demonstrate that cortisone or Compound F (hydrocortisone) reduced the penetrability of this antibiotic.

Cortisone orally seemed to help in the present case. It definitely did no harm. However, cortisone certainly would not be the drug of choice in a case of intraocular infection. The antibiotic should be used first. If the antibiotic does not show any therapeutic effect, cortisone may actually be dangerous because it may diminish the ability of the body to localize the infection and may reduce antibody response as well.

Typhoid-fever therapy and antibiotics

Typhoid-fever therapy was the principal agent against postoperative endophthalmitis before the advent of the sulfonamides. It produces fever and leukocytosis and mobilizes the defenses of the body. It may increase the effect of other agents. With the sulfonamides, it must, of course, be used with caution because fever and dehydration increase the hazard of kidney affection. A final decision on combined treatments rests with the future.

Summary

A case of endophthalmitis following cataract extraction is presented. Although not much vision was preserved, the eye was saved and it is felt that oral chloramphenicol was instrumental in this. It should be the drug of immediate choice in endophthalmitis secondary to cataract extraction and used until cultures indicate some other therapy. Although the use of cortisone with antibi-

otics definitely did no harm in my case, the role of cortisone in intraocular infections has not, as yet, been determined. The combined use of intravenous typhoid and the antibiotics or chemotherapeutic agents may be effective in intraocular infections.

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A NEW APPROACH TO THE PTERYGIUM OPERATION*

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The pterygium is first dissected from the cornea according to this technique:

The separation is begun at the neck of the pterygium by means of a spatula inserted under the pterygium tissue at the limbus either from above or below. Reaching below the margin (or superior margin) the end of the spatula comes out on the conjunctival surface. With a sawing motion it is moved gradually toward the head and body of the pterygium. Dissection, without the use of a knife, must be done as widely as possible. The head of the pterygium which, as is well known, is always firmly attached to the cornea, is held with forceps, lifted, and severed with a keratome.

It is very important not to leave a particle of pathologic tissue on the cornea. In order to remove small pieces of the pterygium tissue, use scissors with fine sharp points, pressing them on the corneal surface. After complete removal, one-percent Pyoctanin is applied to the corneal wound.

The body portion of the pterygium is also dissected up from the sclera to an area far from the limbus. The dissected tissue is never cut off but folded back as far as possible from the cornea; extirpation sometimes causes keloid of the globe. My favorite procedure is to incise the pterygium lengthwise into two parts which are implanted obliquely above and below according to Knapp's method. In the case illustrated in the figures of this paper, however, the flap is simply turned inside out and fixed with one suture.

It must be repeated that every particle of pathologic tissue must be completely removed from the wound surface where the pterygium was attached, whether it may be cornea or sclera.

Next the conjunctival bridge is made. To do this, an incision is made in the conjunctiva (fig. 1-bbb) 1.5 mm. outside and around the limbus. Next, a conjunctival incision is made (fig. 1-cc) on the side opposite the pterygium parallel to and three mm. outside the limbal incision (fig. 1-bbb). The length of this incision is a little less than half

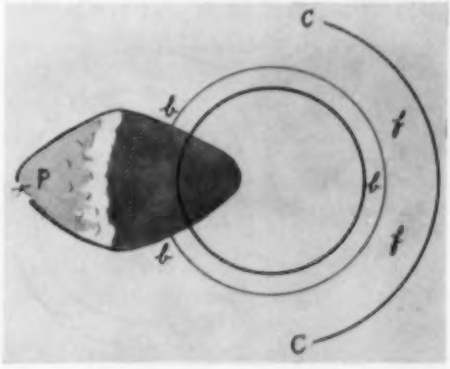

Fig. 1 (Sato). (P) Pterygium. (bbb) An incision is made in the conjunctiva around the limbus. (cc) A conjunctival incision is made opposite the pterygium. (ff) A bridgelike flap of conjunctiva is dissected from the subconjunctival tissue.

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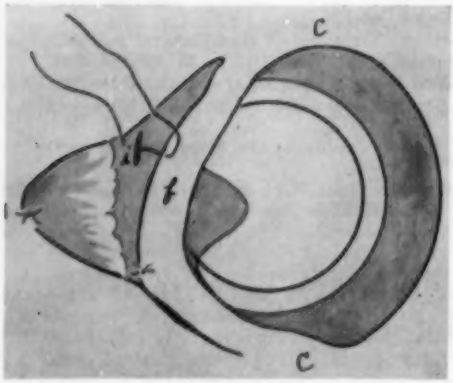

Fig. 2 (Sato). (i) Planned, short, shallow incisions are made in the sclera to expedite suturing.

the circumference of the limbus. It is always best, at first, to make it shorter than the intended length and add to its length as needed when suturing. By raising with a spatula and using scissors, the bridgelike flap of the conjunctiva (fig. 1-ff) is dissected from the subconjunctival tissue. The flap must be peeled as thinly as possible.

This bridgelike conjunctival flap is then transplanted to the surface of the wound from which the pterygium has been removed as shown in Figure 3, and is attached with very fine sutures to the sclera at two or three places. If planned short, shallow incisions have been made in the sclera (fig. 2-i) suturing can be carried out easily by hooking the edge of the incision with the needles. (Of course, transplantation must be done after complete hemostasis.) Finally, the larger wounds on the temporal, upper, and lower side of the limbus are sutured (fig. 3), although, since the conjunctival epithelium recovers easily and heals on the wound surface of the sclera, it is not necessary to close every little wound opening.

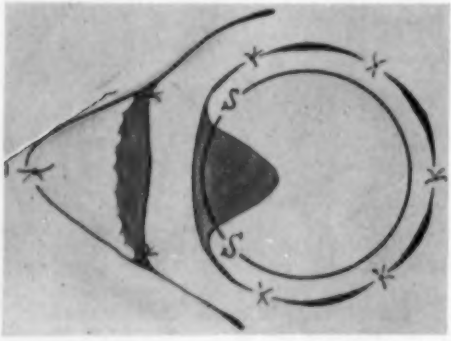

Fig. 3 (Sato). The conjunctival flap is transplanted to the surface of the wound from which the pterygium has been removed.

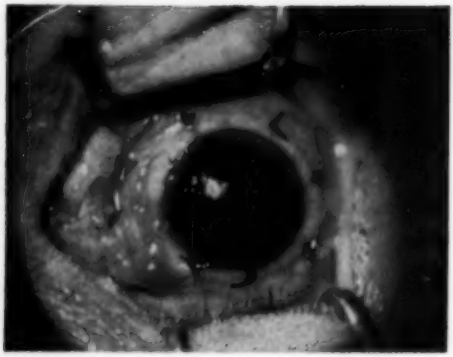

Fig. 4 (Sato). An eye at the completion of the operation.

When the conjunctival flap is too long, some folds develop and more sutures are needed to anchor the points of the flap. This, however, does not present undue complications.

In this method, a portion of the sclera at the limbus, from which the pterygium was removed, is left without a conjunctival covering. This is done because it is ill-advised to have the transplanted conjunctiva superimposed on the cornea. It is better not to cover the sclera exactly up to the limbus. After a week, cortisone (drops and ointment) is started and continued for one month. There is no need for any other special after care.

In my opinion this surgical technique is the best method to prevent regrowth for almost all cases of pterygium. It is especially effective in advanced cases.

Yushima Bunkyoku.

GRAEFE KNIFE INCISION WITH M-SHAPED CONJUNCTIVAL FLAP AND PREPLACED CORNEOSCLERAL-CONJUNCTIVAL SUTURE

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Having tried different types of cataract incisions and sutures, I have finally adopted a combination of Graefe-knife incision with one fornix-based and two large limbus-based conjunctival flaps which permits easy preplacing of a Mendoza-type corneoscleral-conjunctival suture and which has proved simple, safe, and satisfactory.

With the possible exception of the three triangular conjunctival flaps formed, none of the details of this procedure are original. It combines the smoothness of the Graefe-knife incision with the safety of a suture preplaced in resistant tissue and the opportunity to cover the full length of the incision with two large, well-nourished conjunctival flaps.

If covering of the wound is attempted using other types of large limbus-based conjunctival flaps, the preplacement of the corneoscleral suture is difficult and the large single flap may interfere with the visibility of iris and pupil. Flaps based on the bulbar conjunctiva have to be anchored in a way which may tend to dislocate the wound edges and may make difficult the introduction of the iris repositor.

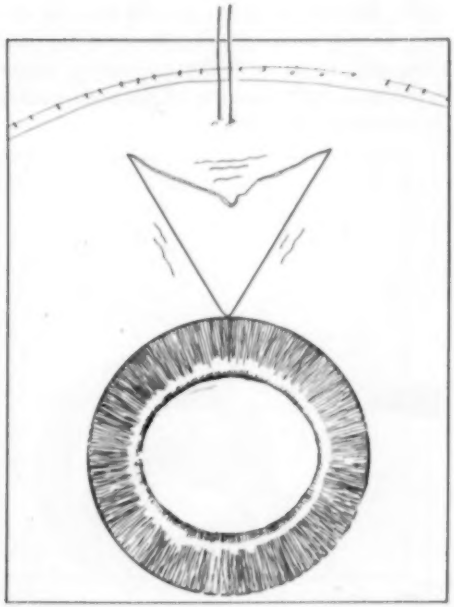

Fig. 1 (Ascher). Conjunctival incision prepares a flap with the tip at the 12-o'clock position.

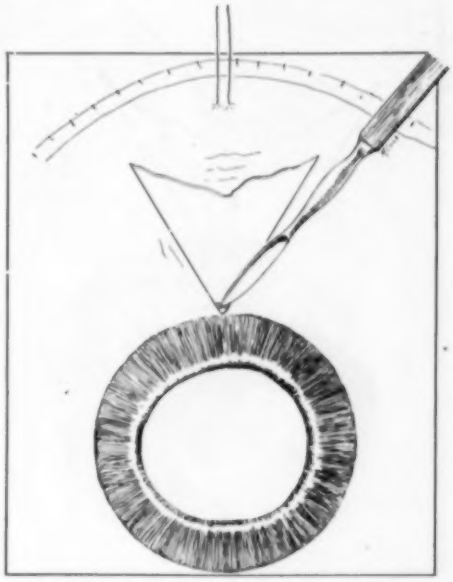

Fig. 2 (Ascher). A groove is prepared for the preplaced suture.

After the usual preparation, retrobulbar anesthesia and akinesis of the seventh nerve, the bridle suture through the upper rectus muscle tendon is introduced and, with straightpointed scissors, a triangular conjunctival flap is dissected starting at the 12-o'clock position at the limbus. From here two diverging cuts extend six to eight mm. upward, the angle between the cuts being about 60 degrees. The flap immediately retracts upward denuding a triangular area of sclera (fig. 1).

A small scalpel is then used to make, at

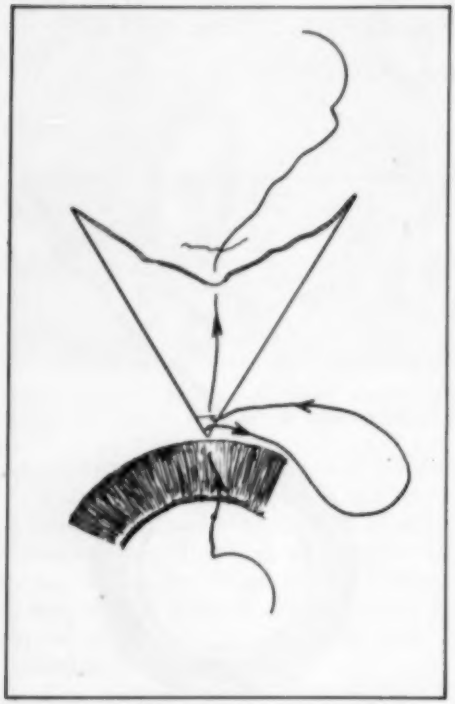

Fig. 3 (Ascher). The suture is introduced through cornea, sclera, and conjunctiva.

the 12-o'clock position, and 0.5 mm. above the limbus, a short slanting incision comprising about half the thickness of the bulbar coat (fig. 2).

Into this groove, a double-armed, 6-0, black braided silk suture with atraumatic three-eighths curve needles is introduced after a knot has been placed at the lower end of the suture to permit quick wound closure in case of emergency. The upper needle is led through the corneal and scleral lips of the prepared groove and finally through the tip of the retracted triangular conjunctival flap (fig. 3). If, during introduction of the suture, the needle is not brought out of the groove and reintroduced into it, the thread must be withdrawn from the groove with a dull hook.

Then, the thread is moistened with saline solution and draped out of the way of the Graefe knife. The latter is introduced at the 3- or 9-o'clock position, aiming toward the opposite limbus. In one act, the half-circle incision and the formation of two triangular limbus-based conjunctival flaps are performed.

Due to the previous preparation of a triangular retracting flap, the Graefe-knife incision cuts two "ears" which, together with the first retracting flap, result in an M-shaped conjunctival incision (fig. 4). When, during further manipulation, these two ears fall back over the limbus, they still permit one to see cornea, iris, and pupil.

Adherent to the limbus between the 9- and 12-o'clock positions and between the 12- and 3-o'clock positions, but open at the 12-o'clock position, this twin-flap enables the surgeon, after removal of the lens, to tighten the preplaced suture easily, to perform the toilet of the iris, and eventually to cover the corneoscleral wound with safety (fig. 5). One 5-0 suture at the tip of each "ear," and two more, halfway between tip and base of the flap, usually suffice to bring the twin-flap into snug apposition with the underlying tissue whereby a tight covering of the deep wound is provided (fig. 6).

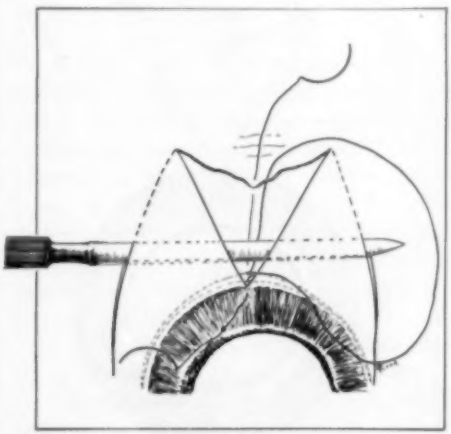

Fig. 4 (Ascher). The Graefe knife performs the limbal section and dissects two limbus-based triangular flaps.

Complications may occur as follows:

1. The groove which is to accept the preplaced suture may turn out to be too shallow or too deep.

If it is too shallow, with the tip of a sharp knife very small scratches should be made on either side of the inaccessible silk thread without touching the latter until the thread can be grasped with a dull hook and drawn out.

If the groove is too deep it may open the chamber and aqueous will slowly escape. In this case, the section should be finished as it would after a keratome incision, using scissors to enlarge the opening in the nasal and temporal direction and, instead of a preplaced suture, the silk must be introduced after the first incision has penetrated into the anterior chamber. Guarded blades may prevent this contingency.

2. The Graefe knife may cut the suture; after this, introduction of another thread through the original channel should be attempted or, if a sufficiently long piece of silk remains uncut, it can be threaded through a small needle and reintroduced through the original stitch canal.

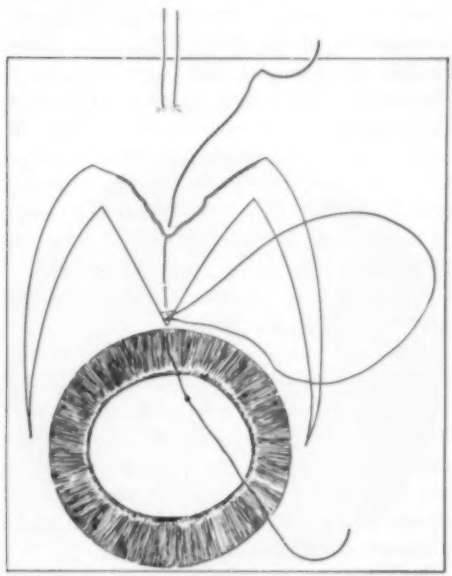

Fig. 5 (Ascher). Appearance of the conjunctival flaps after the section.

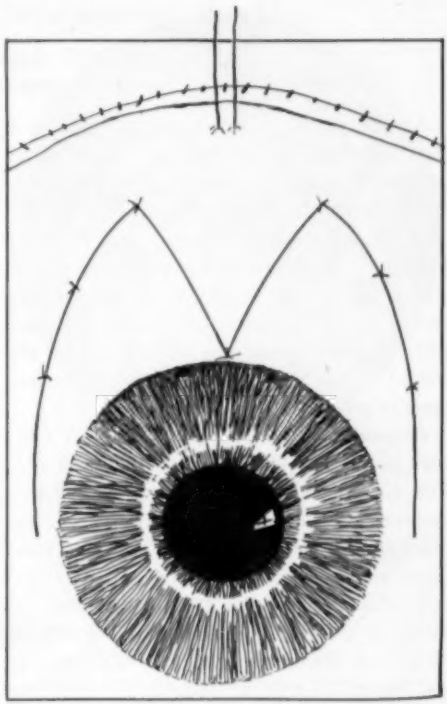

Fig. 6 (Ascher). Appearance of the conjunctival flaps at the end of the operation, after suturing.

Summary

A simple and safe method for closure of the cataract wound by a triple conjunctival flap with a preplaced suture is described and possible complications discussed. Due to its specific preparation, the flap gives easy access to the 12-o'clock position where the preplaced suture is to be introduced, does not obscure the view of iris and pupil and, after being sutured back to its former site, provides both good mechanical wound closure and early restoration of the original blood circulation.

5 West Fourth Street (2)

ARTERIOVENOUS ANEURYSM OF THE RETINA*

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Arteriovenous aneurysm of the retina is a rare lesion and, when found, is most often associated with an aneurysm of the midbrain. Wyburn-Mason,[1] in his classic review of the subject, has collected 27 cases with the arteriovenous lesion of the retina. Of these, 22 had evidence of intracranial aneurysm. Five cases have been reported without other symptoms than those of the retinal lesion. A brief resume of these five cases is given.

Magnus.[2] A man, aged 29 years. A two-year history of visual loss in the right eye. The eye was blind with no direct pupillary reaction. Two direct arteriovenous communications were seen, one superior temporal and the other lower nasal.

Seydel.[3] A man, aged 18 years. Dimness of vision in the left eye. Visual acuity 6/9. A direct arteriovenous aneurysm was seen in the superior temporal vessels.

Rentz.[4] A man, aged 23 years. Failure of vision in the right eye for an indefinite period. Visual acuity 5/35. Direct arteriovenous communication in a mass of vessels just temporal to the disc.

Stokes.[5] A girl, aged 10 years. Marginal blepharitis was the only complaint. Pupils were normal. Visual acuity, 20/15. A direct communication between superior temporal artery and inferior temporal vein, near the disc.

Kravitz and Lloyd.[6] A woman, aged 32 years. No symptoms, discovered on routine examination. Visual acuity, 20/20. Many abnormal vessels scattered over the right fundus, with an arteriovenous communication in the lower portion of the fundus.

In none of these was any follow-up reported to determine the later development of neurologic disease or possible progress of the retinal lesion.

Ophthalmoscopically, there is classically a direct arteriovenous communication between the enlarged and tortuous artery and vein. This is usually found in the temporal retina. In addition, there may be an increase in size and number of all retinal vessels, small areas of retinal pigmentation and degeneration may be found, or there may be saclike dilatations of the affected arteries. Optic atrophy has not been found.

The functional changes in the eye are variable, with the acuity ranging from normal to blindness. The first manifestation of the disease may be sudden visual loss due to vascular break and hemorrhage. The field may be normal or may show defects in the region corresponding to the retinal lesion.

The neurologic changes in those cases with midbrain lesions vary, but typically show a Weber's syndrome (a unilateral third-nerve paresis with contralateral hemiplegia) which may be only partial. Pupillary abnormalities have been found in most cases and nystagmus is present on lateral gaze in half of the cases. Speech disturbance, epileptiform attacks, and systolic murmur over the eyeball on the side of the lesion are found in some cases. Mental changes affecting intelligence and memory are found in nearly all cases. A large number also show various psychotic symptoms.

With the neurologic lesions, the cerebrospinal fluid is usually normal and skull X-ray films only occasionally show abnormalities, which are not constant. Ventriculography and arteriography have been carried out only in a few cases, but have usually shown abnormalities when done. Here again different abnormalities are found.

In a number of patients, angiomas of the face on the side of the affected eye have been

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seen, as have pigmented nevi. Various other congenital anomalies, mostly muscular and skeletal, have been noted: absence of the thenar muscles, facial asymmetry, spina bifida, and contralateral limb atrophy. Wyburn-Mason feels that these vascular malformations are part of a large group of related mesodermal and ectodermal defects and that related anomalies are found in members of patients' families.

Case report

A patient is presented, who has been followed for over nine years for a retinal arteriovenous aneurysm, with no change in the lesion and no evidence of neurologic or mental changes.

History. A white man, aged 28 years, was first seen here in December, 1943, with a complaint of poor vision in the left eye. He had first noticed this about two years before, when he was given a physical examination for employment. He believed the vision had become slightly worse since. The right eye seemed normal and he had no other complaints.

Past history was negative. Family history was negative for epilepsy or other mental or neurologic changes. The patient's parents, siblings, and children had no known visual abnormalities.

Fig. 1 (Riffenburgh). Fundus picture of the lesion in the left eye (December, 1943).

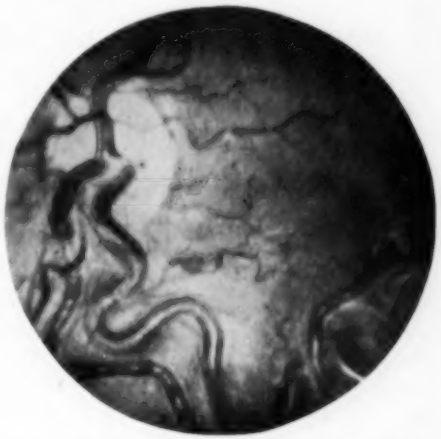

Fig. 2 (Riffenburgh). Fundus picture showing dilated vessels of the disc (December, 1943).

Examination. Vision was: right eye, 6/5, left eye, 6/30. Eyes were externally normal. The pupils were equal and showed normal reactions. Extraocular motions were normal. The cover test was within normal limits. Tension (Schiøtz) was 18 mm. Hg in the right eye and 16 mm. Hg in the left.

Ophthalmoscopic examination of the right eye was negative. The left eye showed minimal edema over the inferior temporal quadrant, where two tremendously enlarged vessels emerged from the disc and took a very tortuous course to end in a tangle of vessels just temporally to and below the macula. The artery and vein were almost indistinguishable. There were a few scattered pigment flecks adjoining the lesion (figs. 1 and 2). Fields showed a defect coinciding with the distribution of the vascular lesion (fig. 3).

General physical examination showed only a palpable spleen. The blood pressure was 110/80 mm. Hg. Neurologic examination showed the cranial nerves intact, except the findings in the left visual field. Reflexes were all present and equal. There was questionable slight hyperactivity of the knee jerks. There were no pathologic reflexes. Sensory

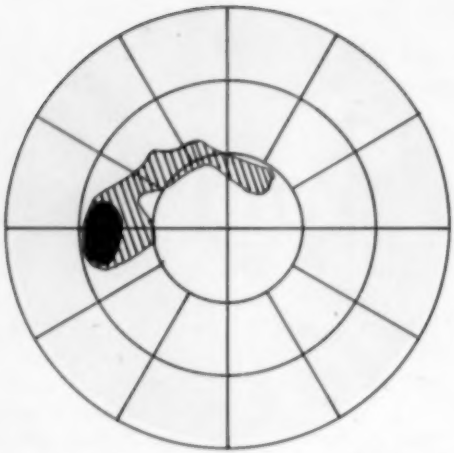

Fig. 3. (Riffenburgh). Visual field of the left eye (December, 1943) with 5/1,000 mm. white.

Fig. 4 (Riffenburgh). Fundus picture of the lesion in the left eye (December, 1952). Compare with Figure 1.

and positional senses were intact.

The blood count was normal. Chest X-ray films showed a peribronchial infiltration, not diagnostic.

The patient was seen several times in 1944 and then was lost to follow-up until December, 1952. At this time the vision in the left eye was 6/60 but there were no other changes in the eye examination. The fields were the same and the fundus picture had not changed (fig. 4).

The physical examination and neurologic examination showed no changes from the previous one. The sensorium was intact and no mental or personality abnormalities could be found. Skull X-ray films were negative.

Summary

Retinal arteriovenous aneurysms are reviewed and the frequent association with aneurysm of the midbrain noted.

A case of retinal arteriovenous aneurysm is presented, which was followed for nine years without evidence of progression and with no evidence of neurologic involvement.

615 First Trust Building (1).

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THE EFFECT OF STREPTOKINASE ON SIMULATED HYPHEMA*

With a study of its toxicity to anterior chambers of rabbits

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Introduction

Hyphema is hemorrhage in the anterior chamber of the eye. It is a serious complication of ocular contusions and injuries.[1]

Hyphema may result in blood-staining of the cornea, usually because of an increased intraocular pressure.[2,3] Blood-staining of the cornea is probably due to the absorption by the corneal stroma of break-down products of the red blood cells in the anterior chamber through Descemet's membrane.[2] The pigmentation of the cornea distorts rays of light coming to the retina, and this results in decreased visual acuity. Blood-staining of the cornea clears slowly and may take as long as two years to resolve completely.[2] Unfortunately, the central or axial part of the cornea is the last portion to clear.

Hyphema is also a complication of cataract extraction, appearing about a week after surgery.[4] The fibrin present may produce an organized exudate which can cover the pupil.[4] Here again the rays of light may be prevented from entering the eye.

Hyphema may be seen after other intraocular surgery, in diabetes and in iridocyclitis.[4] Hyphema is sometimes encountered in buphthalmos and in other diseased eyes, especially following what ordinarily is a minor contusion of the eye.

The treatment of hyphema following contusions consists of bedrest and binocular occlusive patches.[3] Controversy exists as to whether to use miotic or mydriatic drops locally in the eye, or none at all. The miotics may promote reabsorption of the blood by exposing a larger surface of the iris and they may also prevent a secondary glaucoma from developing. Short-acting mydriatics may reduce the possibility of posterior synechias, allay the associated iridocyclitis, and minimize the chance of disturbing an iridodialysis that may be present.

Dr. James N. Greear, Jr., on ward rounds in 1949 at the Episcopal Eye, Ear, and Throat Hospital in Washington, D.C., advised strongly against the use of atropine drops locally when the anterior chamber is completely filled with blood because of the danger of secondary glaucoma. He felt that total or complete hyphema should ordinarily be treated expectantly, using neither miotics nor mydriatics.

Dr. Derrick Vail, on ward rounds in 1953 at Passavant Hospital in Chicago, stated a preference for the use of a miotic (pilocarpine) the first day the hyphema was noticed, with a short-acting mydriatic (homatropine) to be used the following day when the dressing was changed. He was speaking in reference to a partial hyphema following a cataract extraction. He advised alternating the miotic and mydriatic daily until the hyphema cleared.

Payne states that atropine is not necessary and often dangerous to use following nonperforating injuries.[1] Hot packs to the eye may be used to hasten the reabsorption of the hyphema.[4] Operative interference may be necessary to remove a well-organized fibrinous clot which has not cleared in a week or two.[2] Operation to remove hemorrhage may be necessary in hyphema when secondary glaucoma is present and there is an early blood-staining of the cornea.

Streptokinase is a fibrinolytic protein enzyme which can cause human blood clot to resolve and is a growth product of certain

* A thesis submitted to the Graduate Faculty of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Ophthalmology.

strains of the Group A beta hemolytic streptococci.[5]

In 1951, Jukofsky suggested the introduction of streptokinase directly into the anterior chamber to resolve hyphema.[6] He experimented with six rabbits (12 eyes) and found that dosages of 200,000, as well as dosages of 100,000, units of streptokinase were toxic for rabbit eyes. In six rabbit eyes treated with 50,000 units of streptokinase, complete lysis of clots in the anterior chambers took place in three hours with no injury to the eyes.

Jukofsky also reported a human case of hyphema treated with 50,000 units of streptokinase, as well as a human case of subconjunctival hemorrhage. He felt that "the possibilities are promising in hyphema and its treatment and the substance may also prove useful in treating subconjunctival hemorrhages, as well as hemorrhages elsewhere in the eye."

Friedman, in 1952, reported five human cases of hyphema treated with streptokinase.[7] In his experience, the drug was too irritating for use in the human eye; further, he thought that it was not the answer to the problem of intraocular hemorrhage.

As hyphema is still a problem to ophthalmologists, and because of the optimism of Jukofsky's report,[6] this work was undertaken.

Review of the literature

Tillett and Garner, in 1933,[5] first called attention to a substance produced by certain strains of the Group A beta hemolytic streptococci which had fibrinolytic activity. This substance since has been named streptokinase. The mechanism of action of streptokinase[5, 18] and the possibility of its use in hyphema[6, 7] have been discussed.

Streptokinase is a protein enzyme which is a product of and found outside of the cells of the beta hemolytic streptococci.[8] It can be isolated in stable form and resists heating to 100°C. for 60 minutes. Streptokinase is of little use in patients recovering from streptococcal infections because 75 percent of them develop a specific antisubstance against the fibrin-dissolving streptokinase.[9]

Streptokinase has been found to have more fibrinolytic activity against human fibrin clot than against rabbit fibrinogen clot. Whole rabbit plasma clot is resistant to the fibrinolytic action of streptokinase.[5, 6]

Correlation of rabbit experimental results with possible therapeutic results in human hyphema is difficult[6] and probably inadvisable. Streptokinase activates a prefibrinolysin or lysin factor in human serum to produce a fibrinolysin which splits fibrin into polypeptides and thus causes blood clots and fibrinous exudates to dissolve.[10] This lysin factor is present as an inactive precursor or zymogen and may be activated from this state by streptokinase.[11]

Desoxyribosenuclease, hereinafter called streptodornase, is also a protein product of beta hemolytic streptococci which has the power to cause breakdown of desoxyribose nucleoprotein.[13] It is also an enzyme with properties similar to streptokinase. As 30 percent to 70 percent of total purulent sediment is made up of desoxyribose nucleoprotein, streptodornase can liquefy purulent exudates.[13] Streptokinase and streptodornase may be used together, and locally used to treat fibrinous, purulent, and sanguinous exudates[14] and hemothorax.[14, 18] They do not interfere with the concomitant systemic and local use of the sulfonamides or of aureomycin, streptomycin, penicillin, and chloromycetin.[14, 15, 18]

The effect of streptokinase-streptodornase after each local application or injection is limited to about 24 hours.[14]

Cathie found streptokinase to be of help in treating tuberculous meningitis.[15] There is a fibrinous exudate at the base of the brain in tuberculous meningitis and it contains living pathogenic tubercle bacilli. Streptokinase apparently allows streptomycin to penetrate the exudate and, because

of this, better results are obtained.

In Cathie's 14 unselected cases of tuberculous meningitis treated with streptomycin alone, the mortality was 79 percent. In 19 cases treated with streptomycin and streptokinase, the mortality was 42 percent. He found the length of treatment to be decreased with the combined streptomycin-streptokinase therapy.[15]

Streptomycin is effective against hemothorax and streptodornase against empyema.[18] Twenty-seven cases of infected and uninfected hemothorax have been treated with good results. Dosage varied from 100 to 500 units of streptokinase per cc. of chest fluid.

The only toxic manifestations noted in treating exudative pleurisies and hemothorax have been a transient febrile response, general malaise, and a local leukocytosis. These have all disappeared in a few days and have not appeared to damage human tissue or leukocytes.[14, 19] Scar tissue is not affected by streptokinase.[19]

Four to five hundred units of streptokinase are necessary to prevent one cc. of human blood from coagulating.[19] Ten cases of chronic refractory suppuration have been treated.[20] Six cases were chronic osteomyelitis and four were chronic soft-tissue infections. Organisms cultured included Staphylococcus aureus and albus, B. proteus, B. pyocyaneus, and the tubercle bacillus. Streptomycin or aureomycin or chloromycetin were used concomitantly with the application of streptokinase-streptodornase. Draining ceased in six cases.[20]

The results of 85 cases treated with combined antibiotic therapy and streptokinase-streptodornase have been reported. These cases include hemothorax, infected amputation stumps, osteomyelitis, otitis media, decubitus ulcer, actinomycosis, empyema, gangrene, rectal infections, sinusitis, and soft tissue infections. In 80 of these 85 patients good results were reported.[19] The literature concerning this subject is not yet extensive.

Experimental procedure

Preliminary comments

Animal work progressed from May, 1952, through March, 1953, inclusive. Experiments were performed on 22 stock rabbits (43 eyes) weighing about four pounds at the beginning of the work. Frequent observations were made for at least a month on each animal, some being observed over two months. The rabbits were fed natural foods.

The streptokinase in this work was provided through the courtesy of the Lederle Laboratories, Pearl River, New York. It is a combination of streptokinase, 100,000 units, and streptodornase, 25,000 units, per vial. The trade name of this combination is "Varidase." The lot number was 2200-10085. This combination will hereinafter be referred to as streptokinase (after Jukofsky[6]).

Anesthesia was accomplished with 2.5-percent sodium pentothal injected into the ear veins as suggested by Jukofsky.[6] It took about 1.5 to 2.5 cc. of this solution to provide deep initial anesthesia. About the same amount that was injected into the ear vein was then injected subcutaneously to maintain a short period of deep anesthesia. Three rabbits were lost from anesthetic deaths early in the course of the work. It was soon found that, if an overdose was given and respiration failed, a short period of manual artificial respiration restored breathing.

No method has been devised to create by trauma a hyphema which would be fairly similar from rabbit eye to rabbit eye. Therefore, venous blood from the rabbit's ear was injected into its anterior chamber as suggested by Jukofsky.[6] The simulated hyphema thus produced is not like that seen after trauma, where the hemorrhage is from the ruptured intraocular tissues.

Guist forceps were used for fixating the eyes by grasping one of the extraocular muscles near its insertion. This was also done to determine if the initial intravenous injection of pentothal had been sufficient. Injec-

TABLE 1

SUMMARY OF STREPTOKINASE TOXICITY EXPERIMENTS

Rabbit Number	Units of Streptokinase to Right Eye	Toxic Response	Units of Streptokinase to Left Eye	Toxic Response
1	5,000	0	10,000	0
2	15,000	3	20,000	0
3	25,000	1	30,000	0
4	20,000	3	10,000	0
5	26,600	3	20,000	1
6	27,500	1	25,000	0
7	18,750	2	20,000	2
8	20,000	0	20,000	1
9	10,000	0	10,000	0

Grading of toxic response:
0 = None.
1 and 2 = Minor responses which recovered in a few days and no sequelae.
3 = Toxic response with some residual corneal opacification.

tions of both streptokinase and fresh venous blood from the rabbits' ears into the anterior chambers were made with No. 27 intradermal needles (0.5 inch) and tuberculin syringes. The needle was inserted at the limbus nearest the fixated muscles.

PRESENT STUDY

The experimental work is divided into two parts.

Part I describes the procedure and results of the experiments to evaluate the toxicity of streptokinase on rabbits' anterior chambers. Nine rabbits (18 eyes) were used in Part I.

Part II describes the procedure and results of experiments designed to test the efficacy of streptokinase in resolving venous blood from the rabbit which has been introduced directly into its anterior chamber. This latter will be referred to hereinafter as "simulated hyphema." Thirteen rabbits (25 eyes) were used in Part II. The production of the simulated hyphema is described in Part II, as is the fact that the simulated hyphema in one rabbit's eye was treated by injecting streptokinase into the anterior chamber, while the simulated hyphema in its other eye was the control.

PART I: EXPERIMENTS TO EVALUATE THE TOXICITY OF STREPTOKINASE ON RABBITS' ANTERIOR CHAMBERS

Technique. Streptokinase (100,000 units) and streptodornase (25,000 units) comes prepared as a small amount of white powder in a small vial. It is stored at 4°C. It was found impractical to dissolve the streptokinase (100,000 units) in less than 1.0 cc. of sterile 0.1 normal saline; 0.75 cc. and 0.8 cc. were the smallest amounts of 0.1 normal saline in which 100,000 units of streptokinase would dissolve. The saline was injected into the vial. Only fresh material was used throughout this work.

The volume of these rabbits' anterior chambers was only a little over 0.2 cc.; roughly estimated, 0.22 cc. Before instilling the streptokinase, the aqueous from the anterior chamber was drained off. The amount of aqueous drained off depended upon the dosage of streptokinase which was to be instilled into that eye.

When injecting amounts of streptokinase of 25,000 units to 30,000 units, most of the aqueous first had to be drained off. It was found impossible to inject more than 30,000 units of streptokinase into the anterior chamber without making the intraocular pressure abnormally high. It is possible that after injecting amounts over 25,000 units, the intraocular pressure was somewhat increased.

The results of the toxicity experiments are listed in Table 1. Toxic responses were graded zero, one, two, and three.

Zero was no toxic response. Grades one and two were minor responses that recovered in a few days and left no sequelae. These responses were in the nature of haziness of the cornea, and some neovascular formation on the iris. Dr. F. M. Wilson, of the University of Indiana Medical School in Indianapolis, has told me (1953) that the iris of a rabbit develops neovascularity with little provocation, but that this usually recovers quickly and completely.

Grade three toxicity resulted in severe corneal opacification which was still present from one to two months later.

In five eyes given 10,000 units or less there were no toxic responses. In 13 eyes given from 15,000 to 30,000 units there were toxic responses in nine eyes. Six of these nine eyes became normal again in a few days, but three had the residual corneal opacification already mentioned.

Part II: Experiments testing the efficacy of streptokinase in the treatment of simulated hyphema in rabbits

Technique. The simulated hyphema was produced by injecting fresh (unclotted) venous blood from the rabbit's ear veins into its anterior chamber. About 0.15 to 0.2 cc. of blood was mixed with the aqueous by pumping the plunger of the 1.0 cc. tuberculin syringe back and forth.

As much blood was left in the anterior chamber as was consistent with not making the eye unnaturally hard. The eyes were tested for hardness by manual palpation through the lids.

The hyphema in each eye was then examined for uniformity. If the hyphema in the two eyes was not quite uniform, the streptokinase was injected into the eye with the more dense hyphema. This was a separate step and was done within two or three minutes after producing simulated hyphema in each rabbit eye. (Jukofsky injected the venous blood from the rabbit's ear and the streptokinase together, mixing the two before they actually entered the anterior chamber.[8]) When possible, I used the tract of the former limbal paracentesis for injecting the streptokinase.

The results of this work are summarized in Table 2.

In 12 control eyes with hyphema alone, the blood disappeared in from three to 29 days, or an average of 13.2 days. Three of the 13 eyes (one eye each of rabbits 10, 14, and 17) treated with streptokinase became hard to

TABLE 2

Treatment of simulated hyphema in thirteen rabbits

Rabbit Number	Control Eye: Number of Days for Hyphema to Disappear	Units of Streptokinase Used in Treated Eye	Treated Eye: Number of Days for Hyphema to Disappear	Estimate of Response of Treated Eye Compared to Control Eye
10	19	1,000	10	better
11	29	300	9	better
12	12	2,000	21	worse
13	17	2,500	6	better
14	8	1,000	18	worse
15	27	4,000	¼	better
16	11	4,000	11	no diff.
17	9	4,000	7	no diff.
18	no control	4,000	11	no diff. than average control
19	11	5,000	12	no diff.
20	5	3,700	3	no diff.
21	8	5,000	6	no diff.
22	3	3,700	11	worse
Average	13.2		9.6	

palpation within a few hours.

The corneas of these three animals became opaque and the scleras injected, especially about the corneas. These conditions gradually became better over a period of weeks but, though the eyes again became normally soft to palpation, some corneal opacification remained. The same conditions occurred in three of the 12 control eyes (one eye each of rabbits 11, 13, and 15).

As stated in Part I, no toxicity was found upon injecting 10,000 units of streptokinase into anterior chambers. The dosages used to treat the hyphema ranged from 300 to 4,000 units, the average of these being about 3,100 units.

Furthermore, opaque corneas and injected scleras developed in three eyes with hyphema that received no streptokinase, so the streptokinase could not have had anything to do with these conditions in three eyes, and most probably not in the other three.

It was postulated that an acute congestive glaucoma developed in these six eyes secondary to the injections of venous blood; the presumed mechanism being that, on injecting venous blood into the anterior chambers, the increased intraocular pressure in some eyes forced rabbit blood cells into the drainage channels of the anterior chambers. Others have recently reported a similar experience.[21]

The hyphema in the treated eyes disappeared in an average period of 9.6 days. This is not a significantly shorter time than in the control eyes.

Estimates were also made in each rabbit as to whether the treated eye cleared of hyphema appreciably more quickly than the control eye. In 12 rabbits with a control, no appreciable difference was noted in five rabbits, in three rabbits the hyphema was longer in clearing than in the control, and in four rabbits the treated hyphema cleared more quickly than in the control. In one rabbit without a control, the treated hyphema cleared more rapidly (11 days versus 13.2), but the difference was so small when compared to the average clearing of 12 control eyes that no appreciable difference was felt to have occurred.

Discussion

In the amounts of 15,000 units to 30,000 units, streptokinase may produce toxic sequelae when introduced into anterior chambers of rabbits. Ten-thousand units or less of streptokinase may not be toxic to healthy rabbit anterior chambers.

There seemed to be no significant difference, in 13 rabbits, in the clearing of simulated hyphema in the treated and the control eyes. However, the lack of response of rabbit hyphema to streptokinase does not necessarily mean this treatment will be unsuccessful in human cases. Since clinical hyphema is usually caused by trauma or a disease process, in every human case serious consideration must be given the possibility that additional harm may be caused by the paracentesis necessary to introduce streptokinase into an already sick eye.

Summary

1. The literature concerning the discovery and development of streptokinase and streptodornase is reviewed.

2. Into 13 anterior chambers of rabbit eyes, 15,000 to 30,000 units of streptokinase were injected. In three eyes serious toxic sequelae resulted.

3. Into five anterior chambers of rabbit eyes, 10,000 units or less of streptokinase were injected; none showed any toxic results.

4. In 13 rabbits, simulated hyphema of one eye was treated with streptokinase (with an average dose of 3,100 units), while the simulated hyphema of the second eye served as a control. There was no significant difference between the disappearance of hyphema in the treated eyes and in the control eyes.

Conclusion

It is my opinion that much smaller doses

should be used if further attempts are made to resolve hyphema by injecting streptokinase in the anterior chamber; probably less than 5,000 units. If streptodornase should be introduced concomitantly with an antibiotic in an attempt more effectively to treat an endophthalmitis localized in the anterior chamber, the dosage should probably be under 1,200 units.

Veterans Administration Hospital.

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Ophthalmic Miniature

Bean pods are noisiest when dry,
And you always wink with your weakest eye.
Francis Bret Harte, *Tale of a Pony*, 1870

MEASURING VELOCITY OF FLOW IN AQUEOUS VEINS*

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Charged with investigation of the amount of aqueous humor visibly eliminated by aqueous veins compared with the amount of aqueous humor eliminated as found by tonography, we (Stepanik and Kemper, to be published) were faced with the problem of measuring the speed of flow in the aqueous veins.

The first attempt to estimate the amount of fluid visibly eliminated by the aqueous veins was made by Ascher.[1] Instead of diameters of aqueous veins, Ascher used Leber's measurements of conjunctival veins and Theobald's[2] figures for the diameters of the deep outlets of Schlemm's canal, and tentatively assumed that Zeller's[3] estimations of velocity of flow in conjunctival veins (between 0.7 to 1.8 mm./sec.) might roughly correspond to that in aqueous veins. Using these figures and the formula:

$$\text{Minute volume} = \pi \text{ (major semiaxis) (minor semiaxis) (velocity)}$$

Ascher reached an approximate accord between the amount of fluid eliminated by aqueous veins and estimations based on different methods, published by other authors.[4]

De Vries[5] attempted measurement of the actual velocity in aqueous veins by following the course of tiny waves of red blood cells, shooting through the aqueous veins. These red-cell waves, rhythmically entering an aqueous vein, were first described by Ascher;[1] he found that they generally arrive in the intervals between two radial pulse beats.

De Vries, calling these blood-cell waves "projectiles," compared the time needed for them to pass a previously measured vessel section with the time between two pulse beats. Due to the fact that the red blood-cell waves are not found in every aqueous vein, De Vries ascertained the velocities in but four of his numerous subjects and found them to be 1.5, 3.3, 3.5, and 7.5 mm./sec.

Using these figures and the measured widths of the aqueous veins, he calculated the amount of fluid leaving the anterior chamber, and arrived at values similar to those published by Ascher and by previous investigators.

We could have tried to measure the velocity of the red blood cells in aqueous veins by the procedure of Basler,[6] who determined the speed of flow in the capillaries of the nail bed, a method dating back more than 30 years and also used by Zeller[3] for the blood vessels of the human conjunctiva. However, the following method seemed to be suitable.

METHOD

On considering the mechanism of the pulsating blood waves which enter aqueous veins, I devised a relatively simple method of producing such projectiles artificially. Clear aqueous veins often show minute tributaries supplying small amounts of blood at low speed (fig. 1-a). If gentle compression is exerted proximally from the entrance of such a minute vein, using a bent Bowman probe (fig. 1-b), the intravascular pressure inside the aqueous veins will suddenly drop for a moment and will permit the entrance of more blood into the aqueous veins during this period of decreased intravascular pressure.

As soon as compression is released, the previous pressure gradients become re-established, further entrance of blood from the tributary is restricted to its original trickle, while the "projectile" formed during the period of reduced aqueous humor pressure is

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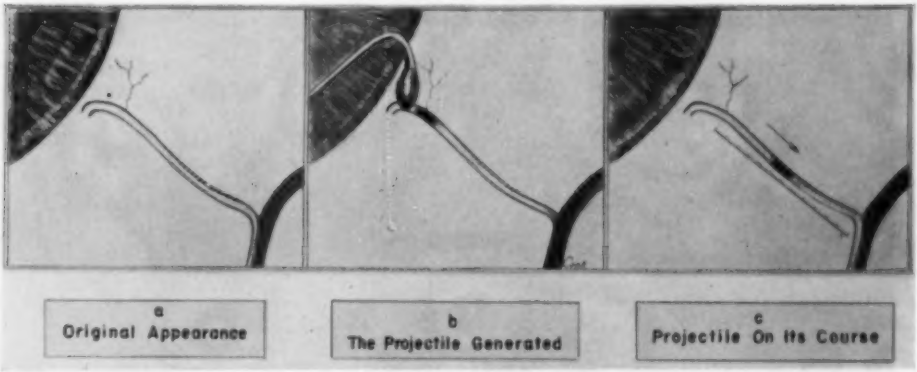

Fig. 1 (Stepanik). Production of "projectiles" in a clear aqueous vein by touching it upstream from its junction with a small venous tributary.

being carried on with the aqueous stream (fig. 1-c). A short touch suffices to produce the projectile; prolonged compression would allow entrance of a longer cylinder of blood.

With the help of Mr. F. H. Eastabrooks, we succeeded in photographing one of these projectiles on its way through the aqueous vein, corresponding to the sketch drawn in Figure 1-c. Figure 2A shows the aqueous vein clear, prior to compression. Figure 2B shows the same vein with the projectile passing.

It is interesting that, even in aqueous veins without visible tributaries, short gentle compression produced projectiles of red blood cells. Although less clearly outlined, these cell clusters could be used for estimation of the velocity as easily as those coming from superficially visible tributaries.

These swarms of red blood cells, emerg-

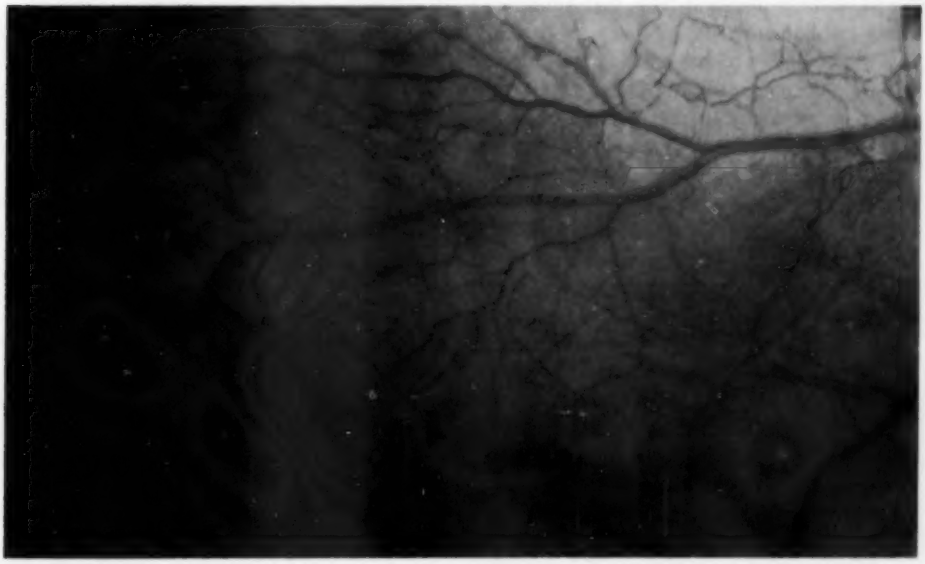

Fig. 2A (Stepanik). Clear aqueous vein, prior to compression.

Fig. 2B (Stepanik). The same vein with the projectile passing. (P) Projectile. (PB) Metal probe.

ing out of the scleral tissues, most probably originate from intrascleral blood vessels and the relatively long way they have to pass before reaching the surface explains why their borders are less sharply outlined as compared to those deriving from tiny superficial venous tributaries.

All projectiles disintegrate after having passed a certain length of the vessel; the higher the velocity in the observed aqueous vein, the shorter is the distance between the points of appearance and of disintegration of a projectile. While the compression produces a short stoppage of flow, no change in distribution of blood and aqueous was observed after cessation of the compression and disappearance of the projectile.

Our measurements were performed without the use of anesthetics.

Main sources of error in estimating the velocity by this method include the inexactness of measuring the time and the distance travelled by the projectile. Aqueous veins shorter than one mm. were not used at all. The error in measuring length was estimated as ± 0.02 mm. In most cases, the time was less than one second. The times reported in the table are the averages of three separate measurements. Using a stop-watch with scale marked in tenths of seconds, we might have made errors of ± 0.1 second. Therefore, the errors in timing are the more serious.

Another error, difficult to be evaluated, is the disturbance of the natural conditions of current and pressure produced by compression of the aqueous vein. In three preliminary experiments, I compared the velocities of spontaneous blood cell waves with those of artificially produced projectiles in the same vessel, and the values were identical in both cases.

Results

I attempted to measure the velocity of current in 67 aqueous veins of 30 normal eyes. In 60 of these vessels, projectiles could be produced by the method described above; five aqueous veins were too short and two were situated so deeply that observation was difficult. The velocities found for the 60 aqueous veins of 30 normal eyes were between 1.3 and 7.6 mm./sec., with an average

TABLE 1

VELOCITY OF FLOW IN AQUEOUS VEINS OF NORMAL EYES

Eye No.	Aqueous Vein No.	d mm.	l mm.	t sec.	v mm./sec.
1	1	0.050	2.70	0.6	4.5
	2	0.050	1.52	0.3	5.1
2	3	0.050	3.80	1.5	2.5
3	4	0.035	2.28	0.3	7.6
	5	0.035	2.66	0.5	5.3
	6	0.035	1.71	0.3	5.7
4	7	0.070	4.18	0.7	5.9
5	8	0.035	2.28	0.4	5.7
	9	0.050	deep	—	—
6	10	0.035	2.66	0.7	3.8
7	11	0.035	3.80	0.7	5.4
8	12	0.050	3.42	0.5	6.8
	13	0.035	1.14	0.4	2.8
	14	0.050	3.80	1.5	2.5
	15	0.035	short	—	—
9	16	0.050	1.52	0.2	7.6
	17	0.035	2.28	1.0	2.3
10	18	0.050	3.80	0.5	7.6
11	19	0.050	1.33	0.2	6.6
12	20	0.050	2.66	0.4	6.7
	21	0.050	3.04	0.6	5.0
	22	0.035	1.71	0.3	5.7
13	23	0.035	1.90	0.3	6.4
	24	0.035	1.71	0.3	5.7
	25	0.035	1.90	0.5	3.8
	26	0.070	4.56	0.7	6.5
14	27	0.035	2.09	0.4	5.0
	28	0.035	1.14	0.8	1.4
	29	0.050	3.23	0.7	4.6
	30	0.050	3.80	0.8	4.7
15	31	0.070	3.61	0.8	4.5
16	32	0.035	short	—	—
	33	0.070	1.52	0.4	3.8
	34	0.050	2.09	0.4	5.0
17	35	0.050	3.04	0.8	3.8
	36	0.036	2.66	2.0	1.3
18	37	0.050	3.80	1.5	2.5
19	38	0.070	3.80	0.7	5.4
	39	0.050	1.52	0.3	5.0
20	40	0.035	deep	—	—
	41	0.050	3.04	0.6	5.0
	42	0.035	2.85	0.6	4.7
	43	0.035	2.28	0.6	3.8
	44	0.050	2.66	0.5	5.3
21	45	0.035	2.28	1.1	2.0
	46	0.035	short	—	—
	47	0.050	3.42	0.8	4.3
22	48	0.050	3.04	0.5	6.0
23	49	0.035	1.52	0.5	3.0
	50	0.035	1.71	0.5	3.4
24	51	0.035	1.52	0.3	5.0
25	52	0.035	1.33	0.3	4.4
	53	0.050	1.90	0.5	3.8
	54	0.035	short	—	—
26	55	0.035	2.40	0.8	3.0
27	56	0.035	2.28	0.4	5.7
	57	0.035	2.66	0.6	4.4
	58	0.050	short	—	—
28	59	0.025	3.42	1.0	3.4
	60	0.070	3.04	1.0	3.0
	61	0.035	3.80	1.0	3.8
29	62	0.050	3.80	0.6	6.3
	63	0.035	2.65	0.5	5.3
	64	0.070	3.42	1.7	2.0
	65	0.025	2.28	0.7	3.2
30	66	0.050	4.00	0.8	5.0
	67	0.035	4.56	0.7	6.5

d = Width of aqueous vein in mm.
l = Length of measured section of aqueous vein.
t = Time required by projectile to pass through.
v = Velocity of the projectile in mm./sec.

velocity of 4.6 mm./sec. (table 1).

The average error was 19.2 percent, the lowest being estimated at five percent and the highest at 50 percent. There seems to be no correlation between vessel diameter and speed of current in the aqueous veins.

In the same eye, the velocities vary considerably from aqueous vein to aqueous vein.

Discussion

In streamline flow through very small vessels the movement of fluid takes place in lamellae paralleling the vessel walls. It is well known that in this case the velocity is greatest along the axis of the capillary and decreases parabolically to zero at the vessel wall. It is also known that the axial velocity equals twice the average velocity; that is, $v_{max} = 2v_{av}$.

If the projectile diameter were very small as compared with the vessel diameter, the speed of the projectile would be only slightly less than the axial velocity. At the other extreme, if the projectile diameter equals the vessel diameter, then the velocity of the projectile would equal the average velocity in this vessel.

According to my observations and the drawings published by De Vries[5] the projectile diameters are, if not equal to the vessel diameters, at least not very much smaller. It is therefore probable that the observed projectile velocities are closer to the average velocity than to the axial velocity.

Two additional factors, not already considered, may influence the results, namely, the change in pressure in the vessel due to compression when the projectile is being produced, and the plugging effect of the projectile. These factors probably act in opposite ways and may or may not balance each other. The relative effects are difficult to evaluate. It would seem, therefore, that at the present time the closest approximation is to use the velocity of the projectile as the average velocity of the flow in the vessel observed.

Summary

In a great percentage of aqueous veins it is possible to estimate the velocity of the current by observation of artificially produced projectiles of blood cells. In aqueous veins of 30 normal eyes, the values were between 1.3 and 7.6 mm./sec. with an average of 4.6 mm./sec. These values are well in accord with those obtained by De Vries. The average error of my measurements was estimated at 19.2 percent. The results are discussed in connection with the laws of streamline flow in small vessels.

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I gratefully acknowledge Dr. W. M. Spurgeon's advice in mathematical and physical problems. The drawings from my original sketches were made in the Department of Medical Art, College of Medicine, University of Cincinnati.

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AN EXPERIMENTAL STUDY OF THE EFFECT OF CORTISONE ON THE EYE*

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INTRODUCTION

This paper presents the results of certain studies on the effects of cortisone on the eye. These studies compare the effects of local instillation, subconjunctival injection, and intravitreal injection of cortisone in normal rabbit eyes. They also include the effects of cortisone on the rate of epithelization of rabbit corneas following experimental denudation and on the healing of incised corneal wounds in the rabbit.

When this series of experiments was begun, few investigations had been reported on the choice of methods of administration of cortisone. It had been found by Woods[1,2] that drops of cortisone applied locally to the eye were innocuous in concentrations up to and including 25 mg./cc. Subconjunctival injections were being given patients with anterior segment inflammatory disease with apparently good effect, but no experimental data were presented to substantiate the assumed promise that this method of administration was entirely innocuous. The possibility of using intracorneal and intravitreous injections in certain disease conditions suggested that these methods of administration should also be investigated in the experimental animal.

The advantages of the local use of cortisone are obvious. Drugs applied locally may be maintained at much higher concentrations and at much less expense than is possible by systemic administration. Local administration also avoids side effects of cortisone which occur when it is given systemically and which may contraindicate its use in certain patients. It was felt, therefore, that various methods of local administration should be experimentally evaluated.

EXPERIMENTAL STUDIES

PART I: EFFECTS OF CORTISONE APPLIED LOCALLY TO THE EYE

A. LOCALLY INSTILLED DROPS

Cortisone drops in concentrations up to 25 mg./cc. were found to be innocuous to the rabbit eye, confirming the previous observations of Woods, and this method of administration was not further pursued.

B. SUBCONJUNCTIVAL INJECTION

One of us (Scheie) observed a patient who had received subconjunctival injections of cortisone over a period of a week. The conjunctiva was found to be inflamed, bound to the sclera, and in several places white areas were noted which were thought to be deposits of cortisone. As a result of this observation, it was decided to study the effect of repeated subconjunctival injections of cortisone on normal rabbit eyes.

Three rabbits were given 1.0 mg. of cortisone in 0.2 cc. of saline plus the commercial diluent subconjunctivally in each eye for 14 days. Three rabbits were used as controls and given 0.2 cc. of a mixture of diluent and physiologic salt solution, using the same concentration of diluent as in the first group. One cortisone-treated animal died prior to completion of injections. The remainder showed white areas thought to be cortisone deposits and markedly dilated vessels at the end of one and two weeks (fig. 4). The control eyes showed dilatation of vessels only (fig. 2). The animals were then killed and the eyes examined histologically.

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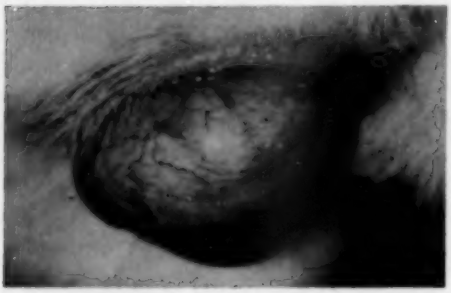

Fig. 1 (Yasuna, Ojers, Frayer, and Scheie). Daily injections of physiologic salt solution for two weeks. Photograph taken at the end of the second week.

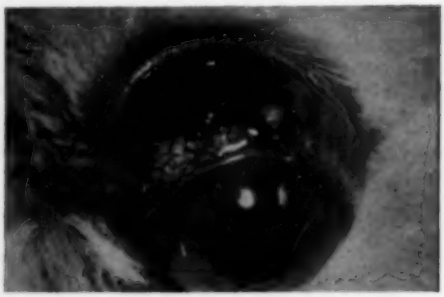

Fig. 3 (Yasuna, Ojers, Frayer, and Scheie). Daily injections of cortisone in physiologic salt solution for 14 days.

The cortisone-injected eyes revealed that the white areas noted grossly were in reality abscesses, incited by the retained cortisone. These were typical in that there were dilated vessels, central necrosis, heavy infiltration of leukocytes, and early signs of organization at the periphery (figs. 5 and 6). The cellular infiltrate was characterized by large numbers of polymorphonuclear leukocytes containing large eosinophil granules. Bacterial stains were performed from random sections, and failed to reveal the presence of bacteria. No abscesses were found in the control eyes. The only changes noted in the control eyes were varying degrees of diffuse infiltration by acute inflammatory cells, many of which contained large eosinophil granules.

This experiment was repeated with five rabbits, the right eye being injected with cortisone in saline subconjunctivally, and the left with diluent in physiologic salt solution subconjunctivally. The results were essentially the same as in the previous experiment (figs. 2 and 3).

The results indicate that cortisone injected subconjunctivally may produce sterile abscesses, and that neither the commercial diluent or physiologic salt solution can be incriminated.

C. Intracorneal administration

Four rabbits were used. The left eye of each rabbit was given an intracorneal injection of 0.1 cc. of a cortisone suspension (0.5 mg.) in physiologic salt solution. The right eye, used as a control, was given 0.1 cc. of diluent in physiologic salt solution. Daily observations were made on these eyes.

Fig. 2 (Yasuna, Ojers, Frayer, and Scheie). Daily injections of physiologic salt solution and commercial diluent for 14 days.

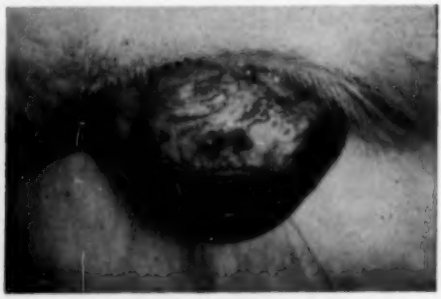

Fig. 4 (Yasuna, Ojers, Frayer, and Scheie). Daily injections of cortisone and commercial diluent for 14 days.

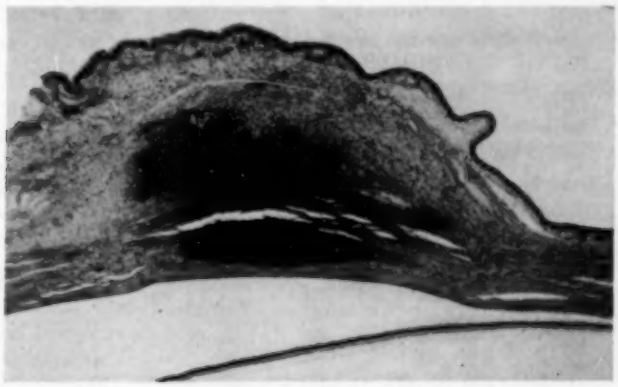

Fig. 5 (Yasuna, Ojers, Frayer, and Scheie). Microphotograph of one abscess seen in Figure 3.

All the corneas were hazy immediately after injection. In eight hours a considerable portion of the haze had cleared so that small deposits of cortisone were noted in the cortisone-injected eyes. One cortisone-injected cornea cleared grossly in four days, and the other three cleared in 10 days. Three of the diluent-injected corneas had cleared grossly in 10 days, but one cornea was still hazy after 41 days.

Examination with a slitlamp microscope revealed haziness of all corneas after apparent gross clearing. Results indicate that intracorneal administration of cortisone or cortisone diluent causes permanent clouding of the cornea (table 1).

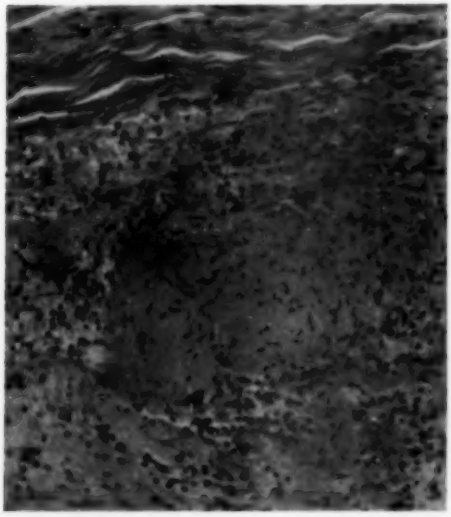

Fig. 6 (Yasuna, Ojers, Frayer, and Scheie). Acute inflammatory response to subconjunctival deposits of cortisone.

D. Cortisone injected into the vitreous

Twelve rabbits were used for this experiment. The left eye of each was given an injection of 1.0 mg. of cortisone in 0.2 cc. of saline into the vitreous, taking care not to injure the lens. The right eye, used as a control, was given 0.2 cc. of diluent of physiologic salt solution.

Ophthalmoscopic examinations of the media were made daily through an atropinized pupil.

On the first day after injection, several small white areas were noted in the vitreous of the cortisone-injected eye, which were thought to be cortisone deposits. After six days these deposits had absorbed. The vitreous remained hazy in five of the 12 cortisone-

TABLE 1

Cortisone injected into the cornea

	Gross Examination	Slitlamp Examination
Cortisone-treated	1 clear on 4th day 3 clear on 10th day	All hazy after 41 days
Control	3 clear on 10th day 1 hazy after 41 days	All hazy after 41 days

TABLE 2

EFFECT OF CORTISONE INJECTED INTO THE VITREOUS OF THE LEFT EYE WITH THE RIGHT EYE AS CONTROL

(Duration of observations seven days)

Cortisone treated	7 eyes cleared after absorption of cortisone	5 eyes hazy media
Control	8 eyes remained clear	4 eyes hazy media

injected eyes. Four of the 12 control eyes were left with hazy media.

Results indicate that injection of material into the vitreous may result in permanent clouding (table 2).

PART II: EFFECTS OF CORTISONE ON EXPERIMENTAL WOUNDS

This study was divided into two parts:

A. The effect of cortisone on experimentally produced corneal abrasions.

B. The effect of cortisone on penetrating wounds of the cornea.

The purpose of this work was to determine if cortisone has any effects on corneal wound healing that might either encourage its use clinically or contraindicate its use either postoperatively or after accidental wounds of the cornea.

A. EFFECTS OF CORTISONE ON THE HEALING OF A STANDARD CORNEAL ABRASION

Leopold,[3] in 1951, reported experiments from which he concluded that epithelial regeneration was delayed by the use of cortisone. Ashton and Cook,[4] and Lister and Greaves,[5] could not confirm the work of Leopold except following the administration of very high doses of cortisone, when some inhibition of epithelization appeared to be present. In tissue culture, Steen[6] reported that epithelial cells grow actively without inhibition when exposed to high concentrations of cortisone. In order to pursue this further, the following experiments were performed:

A 4.5-mm. round trephine was used to outline a circle on the cornea. The epithelium was then removed from this area. Ten rabbits were used (20 eyes).

Five rabbits were used as controls and five received cortisone. All animals received daily intramuscular injections of 50,000 units of procaine penicillin per kg. and 0.25 gm. of dihydrostreptomycin per kg. In addition to antibiotics, five animals received 6.0 mg. of cortisone acetate per kg. injected intramuscularly daily.

TABLE 3

SIZE OF UNHEALED AREA OF CORNEA 24 HOURS AFTER A 4.5-MM. ROUND EXPERIMENTAL ABRASION

Cortisone-Treated				Control			
Animal	Eye	Dimensions	Area	Animal	Eye	Dimensions	Area
A	OD	2½ round	4.8 mm.²	F	OD	3 round	6.7 mm.²
	OS	2×3	4.5 mm.²		OS	2 round	3.1 mm.²
B	OD	3 round	6.8 mm.²	G	OD	3 round	6.7 mm.²
	OS	2½ round	4.5 mm.²		OS	2½ round	4.8 mm.²
C	OD	2×3	4.5 mm.²	H	OD	3 round	6.7 mm.²
	OS	2 round	3.1 mm.²		OS	3 round	6.7 mm.²
D	OD	4 round	12.0 mm.²	I	OD	3½ round	9.0 mm.²
	OS	3 round	6.7 mm.²		OS	3×2	4.5 mm.²
E	OD	1×2	1.5 mm.²	J	OD	3½ round	9.0 mm.²
	OS	2×3	4.5 mm.²		OS	2½ round	4.8 mm.²
Total			52.9 mm.²				62.8 mm.²
Average			5.29 mm.²				6.2 mm.²
Average Diameter			2.6 mm.				2.8 mm.

After 24 hours none of the 20 eyes had healed.

The areas of remaining abrasion are shown in Table 4. The table reveals a greater average total area healed in the cortisone-treated animals than in the controls. This is not significant, however, because the average difference in diameter is only 0.2 mm. The difference in area healed in the two eyes of the same animal varied from 0.3 mm. to 5.3 mm. in the cortisone-injected animals and from 0.0 mm. to 4.5 mm. in the control eyes. This scatter does not permit any statement to be made regarding the action of cortisone on the healing of experimental abrasions (table 3).

B. Healing of penetrating incisions of the cornea

There is conflicting evidence in the literature as to the effect of cortisone on stromal wound healing. Ragan and others,[7] Taubenhaus and others,[8] Potter,[9] Baker and others,[10] Leopold and others,[8] and Parani and others,[11] have reported interference with wound healing with a depression of some of the tissue elements, particularly fibroblasts and collagen.

Castor and Baker[12] applied cortisone to the nontraumatized skin of rabbits and found the histologic structure of treated skin to be modified, particularly in loss of collagenous fibers; other cells of the dermal connective tissue were fewer in number. The tensile strength of sutured wounds in the skin of rats as determined by bursting strength was decreased in cortisone-treated animals (Howes and others[13]).

Newell and Dixon[14] treated fresh corneal transplants of rabbits with subconjunctival cortisone. After the first three- to four-day period, the cortisone-treated eyes did poorly in that more bulging of the graft was present and the graft and adjacent cornea were not clear. Keratoblastic proliferation seemed to be inhibited when the tissues were studied microscopically.

On the other hand, cortisone in therapeutic doses has no inhibiting effects upon tissue cultures.[15,16] The fibroblastic proliferation appears normal. Steen,[6] however, found that growth in the culture could be inhibited by doses in excess of 25 times the usual therapeutic levels.

Cole and others[16] have run serial sections on biopsies of abdominal wounds in dogs with and without cortisone therapy (2.0 mg. per kg.). They have been unable to demonstrate differences in wound healing.

Ashton and Cook[4] found inhibition of fibroblastic activity in the cornea marked but not absolute. The amount of inhibition was related to the amount of cortisone given. In clinical doses the healing was adequate but less satisfactory than in controls.

Clinically, several reports from the general surgeons[17,18] have indicated no interference with primary wound healing in patients receiving ACTH and cortisone therapy.

Hogan[19] reports the case of an individual with a chronic rheumatic uveitis receiving ACTH and cortisone, upon whom an iridectomy and later a cyclodialysis were done with no interference in healing. Henderson and Hollenhorst[20] report uneventful postoperative healing while the patients were being given systemic cortisone, in one case in which a cataract extraction was done, and in another in which a basal iridectomy was performed.

After reviewing the literature and observing his own cases, Duke-Elder[21,22] is impressed with the fact that the effect of cortisone in small amounts on wound healing is not of such a magnitude that it is contraindicated in ocular surgery.

White male rabbits were immobilized in a small animal holder. The corneas were anesthetized with one-percent pontocaine. The eye was then fixed with toothed forceps, and parallel lines were inscribed on the cornea with a caliper set 7.0 mm. apart. A Bard-Parker lance type blade was then used to incise the cornea between the scratches.

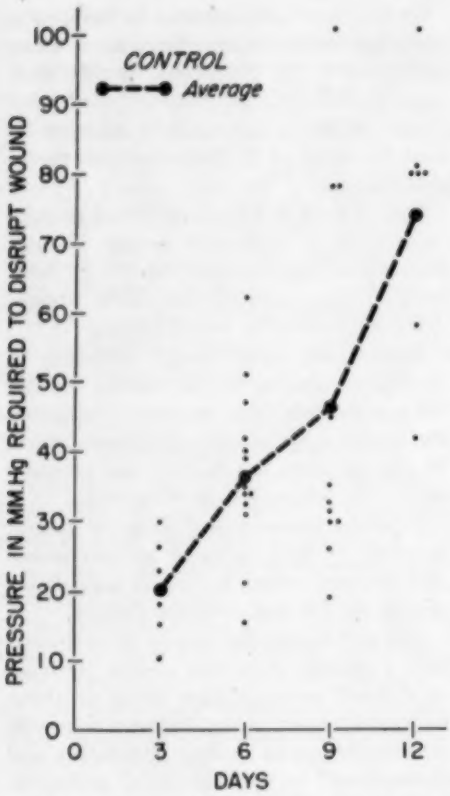

Fig. 7 (Yasuna, Ojers, Frayer, and Scheie). Scatter graph showing the intraocular pressure in mm. Hg required to disrupt a penetrating wound of the cornea at 3, 6, 9, and 12-day intervals (Controls.)

One-percent atropine and 10-percent neosynephrine were then instilled at once. Each animal was given antibiotics as previously described and half received cortisone intramuscularly in the same dose as before.

At three, six, nine, and 12-day intervals, the animals were nembutalized, and a 27-gauge needle attached to a mercury manometer was inserted into the anterior chamber. The pressure inside the globe was then raised, until the wound disrupted. Enucleation was performed, and histologic sections made through the wound.

The pressures required to disrupt the wound were tabulated on graphs (figs. 7, 8 and 9). Inspection of these graphs reveals a wide scatter of results. Averages (fig. 9) fail to indicate any significant difference between control and treated animal.

Histologic sections were taken from a point as close to the central portion of the wound as possible. Serial sections were not made. As an aid in the evaluation, a rough grading of the degree of organization of the wound was attempted as follows:

Grade I, beginning fibroblastic proliferation from the edges of the wound, no fibroblasts completely bridged the wound.

Grade II, bridging of the wound by fibroblasts in the anterior one-half of the wound.

Grade III, fibroblasts bridged the wound

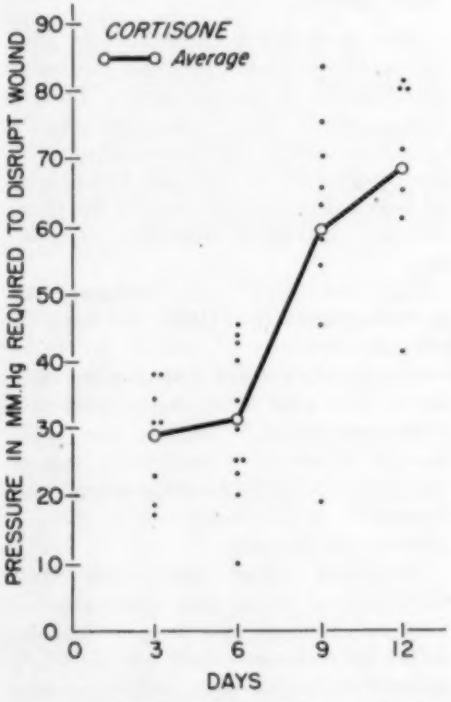

Fig. 8 (Yasuna, Ojers, Frayer, and Scheie). Scatter graph showing the intraocular pressure in mm. Hg required to disrupt a penetrating wound of the cornea at 3, 6, 9, and 12-day intervals. (Cortisone-treated animals.)

both front and back, but were somewhat disorganized.

Grade IV, fibroblasts had become parallel and all traces of fibrin had disappeared.

The number of eyes examined was too small for accurate evaluation of the results; nevertheless, certain impressions seem to be of some significance. There was little difference between the cortisone and control groups at the end of three days. After six days, however, the rate of healing in the cortisone-treated group showed a fairly consistent lag behind the control group. The eyes could be graded about one grade lower than the controls. This same differential held after nine and 12 days (table 4).

It appears, from the two methods of judging wound healing (tensile strength and histologic organization), that controversial points in the literature may be reconciled, that is, histologically there is some inhibition of wound healing, but when judged from the standpoint of tensile strength no significant difference can be noted. We agree with Duke-Elder that when cortisone is indicated postoperatively it can be given with no great danger of interference of wound healing.

TABLE 4

ORGANIZATION OF WOUND

Degree of Organization	0	1+	2+	3+	4+
Control Eyes					
Days					
3	3	1		1	
6		3	9	4	
9			4	9	1
12				5	5
Cortisone Treated Eyes					
Days					
3	6	2			
6	2	6	5		
9		5	6	4	
12			3	9	

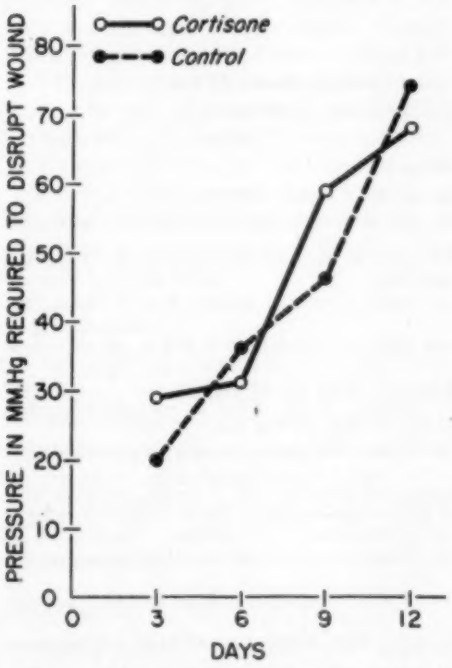

Fig. 9 (Yasuna, Ojers, Frayer, and Scheie). Composite of Figures 7 and 8.

DISCUSSION

Four possible methods of administration of cortisone were investigated in this work. It became apparent very early that intracorneal and intravitreal injection should not be employed for clinical purposes, because of the damaging effect on transparency of the refracting media of the eye. Local instillation of drops into the conjunctival cul-de-sac appeared to be innocuous, and no objections could be raised to the clinical use of this method. Subconjunctival injection, however, did not seem harmless, because abscesses were found at the site of the injection. Since the usual clinical indication for cortisone therapy to the anterior segment of the eye is acute inflammatory disease, it does not seem advisable to superimpose added insult to an already inflamed eye.

Studies of the epithelization of standard corneal abrasions failed to reveal any significant effect on the rate of healing after the systemic administration of cortisone. This appears to be contrary to the findings of Leopold and his co-workers,[3] but in keep-

ing with the results of Ashton and Cook,[4] Lister and Greaves,[5] and Steen.[6]

The results of the effect of cortisone upon the healing of penetrating wounds have some significance. Reports in the literature are somewhat conflicting. Tensile strength studies carried out by us failed to confirm any inhibitory effect of cortisone upon wound healing (figs. 5, 6, and 7). In contrast to this, histologic studies revealed a slight delay in fibroblastic proliferation. Obviously histologic observations serve as a more sensitive indicator of delay in healing than tensile studies but they are, in fact, too sensitive to allow conclusions to be drawn for clinical purposes. The tensile strength experiments indicate that for practical purposes cortisone, in the dosage used here, does not decrease the strength of the wound.

Summary and Conclusions

1. Cortisone instilled locally into the conjunctival cul-de-sac appears to be innocuous in doses up to 25 mg./cc.

2. When cortisone is injected subconjunctivally in a dose of 1.0 mg. in 0.2 cc. of physiologic salt solution daily for 14 days, sterile abscesses are found in the subconjunctival space.

3. Intracorneal and intravitreal injections of cortisone leave the media cloudy.

4. Cortisone does not appear to have any effect on the regeneration of standard corneal abrasions, under the condition of our experiment.

5. Cortisone does not decrease the tensile strength of experimentally produced standard penetrating corneal incisions.

6. Microscopic examination of penetrating corneal incisions revealed a slight delay in fibroblastic proliferation in animals treated with cortisone, as compared with the controls. Slight differences in the degree of fibroblastic repair of wounds show up in histologic sections when they cannot be demonstrated by actual measurements of the tensile strength of the wound. Since this latter is the crucial test from the clinical point of view, it would indicate that cortisone does not inhibit wound healing to an extent which would contraindicate its use.

313 South 17 Street (3).

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CLINICAL PATHOLOGIC CONFERENCE

From the Laboratory of

PARKER HEATH, M.D.
Boston, Massachusetts

CASE E-52-429

HISTORY

The patient, a white man, aged 40 years, gave a history of progressive loss of vision in the left eye, beginning 22 years ago. Three years ago a cataract operation was done in the left eye. He has never had useful vision in this eye. For the past four days the left eye has been red and painful, accompanied by nausea and vomiting.

EXAMINATION

The right eye was white; media clear; fundus normal. Vision 20/30. In the left eye the conjunctiva was congested, cornea somewhat cloudy; anterior chamber shallow; pupil very miotic; iris bulging forward; no fundus details possible; intraocular pressure 50 mm. Hg (Schiøtz); vision nil; transillumination not contributory.

TREATMENT

Strong miotics were employed without demonstrable benefits; in fact, the eye seemed to be adversely affected by miotics and became progressively worse, with more congestion and pain and some rise of intraocular pressure. Enucleation was done for a blind painful eye.

DIFFERENTIAL DIAGNOSIS

*Discussion by Dr. Richard Pippitt**

You can see that there are unlimited diagnostic possibilities. I do not see how any of them can really be eliminated. Could this patient have had a congenital or developmental cataract? I suppose he could. I cannot completely eliminate a corneal cataract which tends to develop around the age of puberty but usually does not progress unless there are complicated factors.

By and large, I would be inclined to eliminate congenital or developmental cataract because of the unilaterality in this patient, the lens in the other eye being completely clear, and because of the progressive tendency. I am assuming that the progressive loss of vision from the age of 18 to 40 years was because

* Assistant at Massachusetts Eye and Ear Infirmary.

of cataract since I have no other information as to what else could have caused it. On the other hand, senile cataract would be unusual at this age.

At the age of 40 years, one naturally thinks of general causes for cataract which, in this case, gives no help. Apparently, the patient is in excellent health, has no generalized disease, no diabetes, no tetany, no general cause for toxins. The unilaterality again would be unusual. Therefore, the causes for this cataract, in the eye itself, are limited.

In this age group, trauma is a frequent cause of cataract, but here we have no history of trauma, and no suggestion is given by the examination of the eye of a perforating injury. I suppose that he could have had a contusion, which occurs with cataract sometimes, or an intraocular foreign body, and a cataract gradually developed, but I think some evidence would be supplied by history or examination.

Other local eye disease could cause the so-called complicated cataract. Nothing here suggests retinitis pigmentosa and, although it could occur unilaterally, we can find no history of it.

There is another cause that could produce cataract in one eye, that is, tumor. I hesitate to think that tumor could persist in an eye from the age of 18 to 40 years and show nothing more than cataract. A long-standing separated retina might be the cause, but again we have no such history.

Inflammation—any uveitis—could cause and often does cause cataract. One particular form of low-grade uveitis and iritis—a heterochromic cyclitis—has to be considered; however, there is no support for this diagnosis.

I hesitate to make a diagnosis. In fact, I cannot make a final diagnosis although I suspect a low-grade uveitis. I wonder whether Dr. Heath will be able to tell us the cause of the cataract, although I predict that he will find a low-grade, nonspecific inflammation. Perhaps we can not learn the exact cause of the cataract. I suppose that the loss of vision was due to the cataract. The history that the patient has never had useful vision in this eye could be interpreted as being before the age of 18 years; however I take it to mean that he has had no useful vision since the operation.

Dr. Heath: This case was sent in for study and the full history, as it was supplied, has been presented here. We are not able to say definitely that the patient had poor vision all his life or just following the cataract operation. I assume what is meant it that poor vision was present an indefinite time before the cataract.

Dr. Pippitt: It could be interpreted to mean anything, but the fact that a cataract was allowed to go on for 22 years could have been the entire cause of the poor vision. At any rate, whether it was or not, why was the cataract operation done at the age of 40 years? The only reason I can think of was that the cataract was producing some complication, and we do have evidence suggesting this.

One complication, a swelling lens, embarrasses the chamber outflow. Other complications are hypermaturity and a toxic effect, with secondary glaucoma or exfoliation of the lens capsule. I rather think the lens became swollen and, because of the rise of intraocular pressure, it was thought best to remove it.

Three years following this operation, and at least four days before examination, the eye became red and painful. At this point a cloudy cornea and shallow anterior chamber were seen. Various miotics tended to increase the difficulty and to increase the pressure.

We are not told anything about the operation—all kinds of complications could have occurred, but there is no description here that the lens ruptured, or that there is any lens material in the eye. All we know is that the chamber was shallow, the pupil was miotic, and the iris tended to bulge forward—a description of iris bombé.

My feeling would be that operation was occasioned by the swelling of the lens, following which a vitreous block developed and that the miotic used only tended to increase the block. The eye was painful and vision nil, and the eye was enucleated.

I shall be interested in hearing the pathologic report. I rather suspect that there is some evidence of chronic uveitis, giant-cell infiltration, cupping of the disc, anterior synechias, and iris bombé, with nothing very specific.

Diagnoses

Clinical diagnosis. Absolute glaucoma, O.S.

Dr. Pippitt's diagnosis. Chronic uveitis, giant-cell infiltration, anterior synechias, iris bombé, and cupping of the disc.

Anatomic diagnosis. Corneal epithelial edema; vesicular keratopathy; pupillary occlusion by lens substance capsule, proliferation of lens epithelium, and fibrous membrane; Soemmerring ring, lens remnants; degenerative changes in iris; low-grade iridocyclitis; operative aphakia; anterior temporal cystic degeneration of retina (marked) and of pars plana of ciliary body; proliferation of pigmented and nonpigmented epithelium; marked peripheral chorioretinitis especially on temporal side; old extensive neuro-epithelial degeneration; early mineralization of retina; uveal and short ciliary proliferative vessels and sclerosis; secondary glaucoma with pupillary occlusion.

Histopathologic presentation

Dr. R. J. Herm†

Gross

Examination of the specimen showed it to be an eye of apparently normal size and shape with a deep anterior chamber, small pupil, no apparent lens, retina in position, and the choroid deeply pigmented. The chief findings were those of a chronic form of long-standing uveitis, mostly posterior, and occlusion of the pupil by lens remnants and subcapsular epithelium.

Microscopic

The cornea showed edema of the basal layers and a defect in the epithelium from a sliding of the epithelium, probably a bullous keratopathy.

Anterior chamber is deep; the angle open. A few red cells and loose pigment are in the trabecular spaces.

Iris and ciliary body show marked degenerative changes and evidences of mild but chronic inflammation, the latter characterized by the presence of some plasma cells, lymphocytes, and plasmacytoid bodies. Posterior synechias are present and formations of intra-epithelial cysts of the pigment epithelium of the iris.

The lens remnants form a Soemmerring's ring and proliferations of the subcapsular epithelium with capsular material extend into the pupillary area. This fibrosis plus a small amount of lens material has occluded the pupil. The presence of pigment in the pupillary membrane indicates that the process is relatively old. The posterior segment shows a well-marked, old, and extensive chorioretinitis with innumerable areas of chorioretinal adhesions, extensive degeneration of the outer layers of the retina, and some mineralization of the retina.

In the retina, the ganglion-cell layer and nerve-fiber layer are fairly well represented, especially at the posterior pole.

Optic nerve. There is atrophy and gliosis of the optic nerve with only slight backward bowing of the lamina cribrosa.

The findings, in summary, are those of long-standing, nonspecific endophthalmitis, chorioretinitis, and loss of neuro-epithelium with relatively recent mechanical complications following cataract extraction. Lens remnants are secondary to cataract extraction. Occlusion and block of the pupil by lens remnants with proliferation of the subcap-

† House officer.

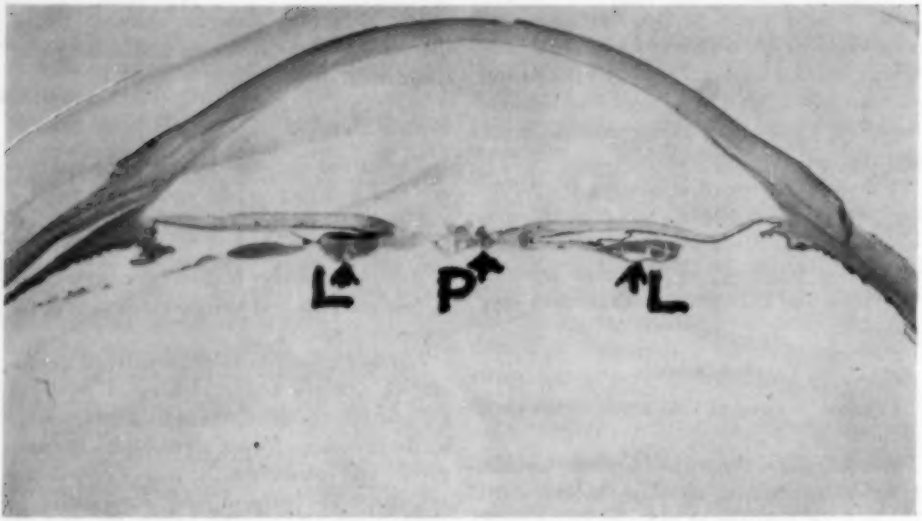

Fig. 1 (Heath). Anterior segment, open angle. (L) Lens remnants (Soemmerring's ring). (P) Membrane, blocked pupil.

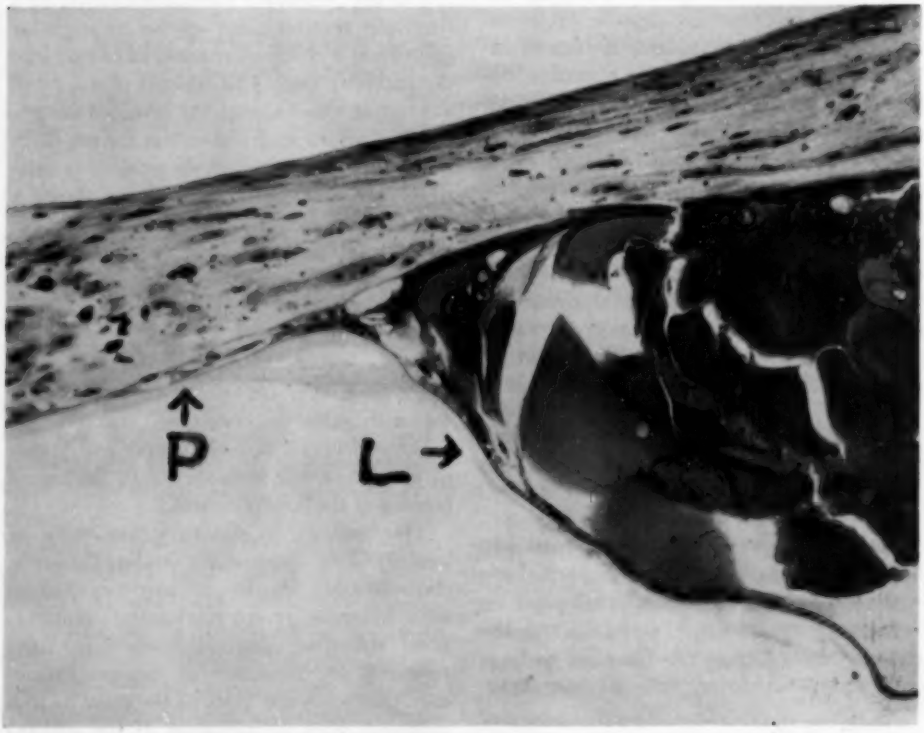

Fig. 2 (Heath). (P) Detail of pupil membrane. (L) Lens remnant.

sular epithelium, capsule material, and fibrous membrane. Acute glaucoma developed, presumably secondary to occlusion of the pupil.

Comments

Dr. Chandler: No peripheral iridectomy? Was this pupillary membrane fibrous in any portion?

Dr. Heath: Yes, dense fibrous tissue, lens substance, and lens epithelial proliferation mixed.

Dr. Chandler: It would be rather unusual for the capsular substance itself to be completely impervious. It would have to have the fibrous tissue added to it to make it watertight.

Dr. Heath: I think the membrane is watertight and clinically bulged anteriorly, but it has dropped back during processing. The evidence is of definite pressure behind pushing the membrane forward.

Dr. Chandler: Could you demonstrate any heterochromia in the iris?

Dr. Verhoeff: There are not any rods and cones left are there?

Dr. Heath: Probably, when the specimen was fresh, a few rods and cones may have been present, but the long-standing recurrent chorioretinitis has done a lot of damage and mostly destroyed the neuro-epithelium. The iris was a darker color than in the well eye.

Dr. Verhoeff: It looks a lot like syphilis.

Dr. Heath: Yes, it looks something like an old chorioretinitis due to syphilis.

Dr. Verhoeff: I don't think I ever saw a case with that in one eye and nothing in the other.

Dr. Heath: I think Dr. Pippitt's suggestion that inflammation was the underlying cause of the cataract is sound. His queries as to whether the patient should have had an attempt at cataract extraction and whether, in the absence of any treatment for glaucoma, enucleation is justifiable, raise important questions. The patient had light perception. It would seem that the pupillary membrane should have been interrupted and the patient given a chance for correction of the glaucoma.

Dr. Chandler: What made the eye blind?

Dr. Heath: I don't think it was blind.

Dr. Chandler: You would think with the nervehead like that it must have been pretty nearly blind.

Dr. Heath: The eye had light perception, but according to the history never had useful vision.

Dr. Chandler: You would think with his angle opening like that, it would have been good enough treatment if he had had a hole made in the iris, and he could have kept the eye.

Dr. Heath: I think that is one lesson from this case. Possibly the eyeball could have been saved. No doubt the advanced state of degeneration from the old chorioretinitis made it hardly worth while to attempt restoration. But such an answer to Dr. Pippitt's query is possible only after the information was available from laboratory study.

Dr. Chandler: One would think he did not have the glaucoma too long.

Dr. Verhoeff: There were no anterior synechias.

Dr. Chandler: That is what makes me think he did not have the block too long. It looks as though he did not get very much atropine.

243 Charles Street (14).

NOTES, CASES, INSTRUMENTS

REPAIR OF SEVERED LACRIMAL CANALICULI*

WITH HYPODERMIC-NEEDLE STYLET WIRES USED AS IN-DWELLING CONFORMERS

RICHARD J. BROGGI, M.D.
Florence, Massachusetts

Many different materials and devices have been used or suggested for use as in-dwelling conformers in the repair of severed lacrimal canaliculi.

The use of a Bowman probe for incised wounds and fresh lacerations is recommended by Spaeth.[1] Callahan[2] obtained favorable results with small sized lacrimal cannulas by inserting the cannula through the lateral segment and then inserting the tip into the medial segment of the severed canaliculus. The use of polyethylene tubing is suggested by Henderson[3] who has used this material successfully in the repair of strictures. Silk[4] and nylon[5] suture material have also been advocated.

Nowhere in the literature could reference be found that stainless steel wire has been used. I have found the use of hypodermic needle stylet-wires from 20G or 21G hypodermic needles very satisfactory and convenient in the repair of lacerated canaliculi.

All of the stylets used in the series reported were stainless steel wires from Becton-Dickinson needles.[6] The 21G stylets measure 0.3 to 0.4 mm. in diameter and vary in length, according to the needles with which they are packaged. The ends are blunt and may be rounded on an oilstone, if desired, prior to insertion into the lacrimal apparatus.

CASE REPORTS

CASE 1

The first occasion for the use of a stylet was in a nine-year-old girl who was admitted to the hospital shortly after sustaining medial and lateral lacerations of her right lower lid on the broken handle of a window. A narrow bridge of tissue separated the punctum from the lateral lip of the medial laceration which completely crossed the canaliculus.

It was obvious that an in-dwelling device as much larger than the punctum as a No. 1 Bowman probe would seriously jeopardize the integrity of the punctum and proximal segment of canaliculus. Consequently, it was decided to use a 21G-needle stylet wire which, with the patient under ether anesthesia, was inserted into the undilated punctum, through the two cut edges of canaliculus and into the nasolacrimal duct.

A 50- to 60-degree bend at about the medial one third of the stylet was manipulated to lie at the junction of canaliculus and lacrimal sac, so that the medial tip of the stylet lay in the nasolacrimal duct. With the stylet in this position, the lacerations were closed anatomically, using a few interrupted 6-0 silk skin sutures; no conjunctival sutures were used.

Throughout the postoperative course, the lid flaps remained in good position, as did the stylet which was bent to rest on the cheek where it was held with cellophane tape. Beginning three days postoperatively, there was no epiphora and on the 12th postoperative day, seven days after discharge from the hospital, the stylet was removed.

Irrigation of the punctum at intervals, including the last clinic visit, which was eight months postoperatively, demonstrated patency of the canaliculus and lacrimal system with the passage of irrigating fluid, without reflux, into the nasal cavity. Epiphora remained absent and an ideal cosmetic result prevailed.

CASE 2

A robust 22-year-old white man sustained a laceration of right lower lid, which completely severed the canaliculus, during a fight.

* From the Eye Clinics of the U. S. Naval Hospitals, Memphis, Tennessee, and Guam, Marianas Islands.

A narrow bridge of tissue separated punctum from laceration.

Under local anesthesia, a 21G-needle stylet was introduced to bridge the torn edges of canaliculus. It was positioned and the wound was closed around it, as in Case 1. In addition, one 4-0 catgut conjunctival suture was used.

There was no epiphora beginning with the fourth postoperative day and the stylet was removed on the 10th postoperative day.

Irrigation tests, as in Case 1, revealed a patent lacrimal apparatus, as late as 11 months postoperatively, which was the last clinic visit. A good cosmetic result was obtained and when last seen, a month later, the patient had experienced no epiphora.

Case 3

Two years after sustaining a superficial laceration that resulted in a scar extending from the medial angle of the right lower lid margin to the cheek, a 19-year-old white man was admitted to the hospital with an acute right-sided dacryocystitis and lacrimal fistula in a scar which terminated, at the lower end, in a draining cheek abscess.

Upon admission, he gave the history of a primary surgical closure of the laceration with subsequent epiphora and recurrent draining abscesses of the right cheek which had cleared, with decreased but not absent epiphora, on two previous occasions with intramuscular penicillin and local hot compresses.

Following admission, the lacrimal sac and entire fistulous tract were incised, with the attendant expulsion of a voluminous amount of purulent material. The fistulous tract was curretted, the lacrimal sac packed with penicillin ointment gauze, and intramuscular penicillin was started. The gauze packing was changed daily and in 10 days all evidence of inflammation had subsided and the fistula had closed.

At that time, a No. 1 Bowman probe could be easily passed from the open lacrimal sac via nasolacrimal duct into the nasal cavity but met impassive resistance at the old scar when attempts were made to pass it into the sac via canaliculus.

Similarly, a 20G-needle stylet met resistance at the same point and, with the stylet abutting against the scar, a small piece of the scar was excised with scissors leaving two cut edges of canaliculus, representing portions which had been medial and lateral to scar. The stylet was then manipulated to lie in the lacrimal system much as in Case 1. The incision was closed with 6-0 interrupted silk skin sutures and the stylet was left in place 14 days.

All medication was stopped two days postoperatively and, after the wire had been in place four days, epiphora ceased completely for the first time in two years. Irrigation of the punctum at intervals for nine and one-half months after removal of the stylet, demonstrated lacrimal-apparatus patency. The wound was well healed at the end of this time and there had been no return of epiphora.

Conclusions

These stylets offer several advantages as conformers. They are not only small enough to be inserted into the undilated punctum without trauma but also, when in position, allow the sphincter punctum to maintain most of its tone. These are particular advantages when only a small bridge of mucous membrane separates punctum from laceration.

The malleability of the stylets is such that they are stiff enough to be passed with facility through the lacrimal passages and yet pliable enough to make easily any number of conforming bends with the fingers and hemostat or forceps.

Their resiliency is sufficient to prevent accidental bending and, once conforming bends have been made, they can only be purposefully removed. The stylets are easily bowed, however, which facilitates their removal after healing has occurred.

In all of these cases, the stylets were intentionally wiggled back and forth daily and in the interims were well anchored to the cheek with cellophane tape.[6] Lid distortion was absent or minimal with the stylets in place and during the daily manipulations. A protective eye shield was used during sleep.

When in position, the stylets cause little or no discomfort. Their lightness, resiliency, and small size would seem to make them relatively immune to physical or pneumatic forces which might otherwise dislodge them. These characteristics also minimize the momentum of the leverage which the external portion exerts against the punctum in instances of undue or inadvertent movement.

SUMMARY

Three cases are presented in which hypodermic-needle, stainless-steel stylet wires were used for the repair of severed lacrimal canaliculi.

It was found that these stylets have several advantageous features and they are offered as a convenient and accessible device for use as in-dwelling conformers in the repair of transected canaliculi.

173 North Maple Street.

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ERYTHROMYCIN*

A REPORT ON A NEW OPHTHALMIC OINTMENT

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AND
WILLIAM A. MOOR, A.B.
Saint Louis, Missouri

New antibiotics are constantly being introduced. Erythromycin is one that has been under laboratory study for several years.[1,2] In general gram-positive, hemophilis, and penicillin-resistant organisms have been found to be susceptible to erythromycin as are some large viruses.[3] The drug has been studied clinically for systemic use.[4,5] The satisfactory use of erythromycin ointment in skin infections has been described.[6] This report attempts an evaluation of the drug as an ophthalmic ointment.

A survey of six ophthalmic ointments including erythromycin (Ilotycin†) is reported. Fifteen consecutive cases of acute bacterial conjunctivitis from the Washington University Eye Clinic were studied by culture and sensitivity studies. These and an additional five cases not cultured were treated with erythromycin ophthalmic ointment.

The bacteriologic method used is a comparison of antibiotic activity for empirical assistance to the physician. It is not to be confused with more refined quantitative and qualitative tests for antibiotic sensitivities that are in common use.

Cultures are taken on specially prepared

* From the Department of Ophthalmology, Washington University School of Medicine, and the Oscar Johnson Institute.

† The Ilotycin ophthalmic ointment was supplied by Eli Lilly and Company.

TABLE 1

SENSITIVITY COMPARISON

Dominant Organisms Isolated from Each Case	Hemolytic Staph. albus	Hemolytic Staph. albus	Hemolytic Staph. albus	Nonhemolytic Staph. albus	Nonhemolytic Staph. albus	Hemolytic Staph. aureus	Hemolytic Staph. aureus	Hemolytic Staph. aureus	Pneumococcoid	Hemophilus	Nonhemolytic Streptococcus	Nonhemolytic Straph. albus	Hemolytic Staph. aureus	Hemolytic Staph. aureus	Pneumococcoid
Mannite broth	+	+	+	+	+	+	+	+	0	0	0	+	+	+	0
Erythromycin (Ilotycin)	6	4	5	5	5	5	5	3	6	10	5	7	5	7	8
Aureomycin	0	2	7	0	5	4	5	5	5	7	6	7	2	6	5
Chloramphenicol	3	0	4	3	4	3	7	5	5	6	3	3	3	3	0
Terramycin	0	0	1	0	2	0	6	3	3	5	4	5	3	3	7
Neomycin	0	0	1	0	1	0	1	0	2	3	2	1	0	2	0
Polysporin	0	0	0	0	0	0	3	0	1	0	0	0	0	0	2
Zinc Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

The numbers indicate mm. growth inhibition on inoculated blood-agar plates.

blood-agar plates and the swabs placed in mannite broth. After incubation, the dominant organism is identified, then emulsified in about 1.0 ml. of broth and a fresh blood agar plate is flooded with the emulsion. Any excess broth is removed and the plate incubated for about 30 minutes (until the surface appears grainy) with the lid tilted to allow excess moisture to escape.

The glass is then marked into pie segments (usually eight to a 3.5-inch plate), and standard loopfuls of the desired ointments are placed on the agar surface of each segment with a control ointment in the center. The plates are incubated and a preliminary estimate made of antibiotic activity after about four hours.

The final reading, a measurement in millimeters of the width of the area of inhibition around each ointment, is made the next day. The preliminary and final readings have always agreed closely.

By this method useful information regarding the antibiotic of choice is available within 18 hours of the patient's first appearance with a complete report the next day.

On the sensitivity comparison chart (table 1) the numbers indicate the millimeters of growth inhibition of each antibody on the infecting organisms. The organisms identified are those falling in the more susceptible zone of the erythromycin antibody spectrum. The following can be noted from Table 1:

Erythromycin alone inhibits in all 15 cases.
Erythromycin is the best in nine cases.
Erythromycin and aureomycin are the best in two cases.
Aureomycin is the best in two cases.
Aureomycin and chloramphenicol are the best in one case.
Chloramphenicol is the best in one case.

Certainly no definite conclusions can be made on such a small series. Erythromycin (Ilotycin) ophthalmic ointment did show the best organism inhibition in this study. That ointment was used in a total of 20 cases of acute bacterial conjunctivitis all of which cleared promptly and satisfactorily. There were no instances of allergic, irritative, or other untoward reaction to that medication.

640 South Kingshighway (10).

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SINGLE INSTILLATION OF CYCLOPLEGIC SOLUTIONS*

RALPH E. TEITGEN, M.D.
Milwaukee, Wisconsin

A safe, nonirritating ophthalmic solution producing cycloplegia after a single instillation would save time for the office assistant and reduce discomfort of patients.

Solutions of methyl cellulose[1,2] and homatropine and of methyl cellulose, homatropine, and phenylephrine were prepared:

	A	B
Phenylephrine hydrochloride	...	1.5
Homatropine hydrobromide	1.5	1.5
Methyl cellulose (4,000-centipoise)	0.3	0.3†
Sodium Acid phosphate	0.08	0.08
Disodium phosphate	0.09	0.09
Sodium bisulfite	0.09	0.09
Chlorobutanol	0.15	0.15
Distilled water to	30.0	30.0

Solution A was instilled into the left eye and Solution B into the right eye of each patient. Patients held the eyes closed for a few minutes following instillation of the drops.

Residual accommodation of each eye was measured by the double blur-point method with a plus three diopter lens. Measurements were made 45, 60, and 90 minutes after instillation of the drops.

Residual accommodation by this method of measuring was assumed to be satisfactory for refraction if three diopters or less remained.[3] Because of the limited number of cases, statistical analysis shown by Brickley and Ogle was not made for these cases.[4]

This series consists of 50 eyes of 25 patients. Twenty-one patients showed satisfactory cycloplegia. Tables 1 and 2 list the data of these satisfactory cases.

Other observations of the satisfactory cases were recorded. The homatropine-ethyl cellulose solution produced slight redness of the conjunctiva of 18 of the 21 eyes. Patients reported the two different solutions produced about equal irritation in the eyes. One patient had equal but only moderate dilatation of the pupils while the other patients had widely dilated pupils. The solution with the phenylephrine produced slightly greater dilatation in eight of the 21 cases. Thirteen patients had hyperopic refractive errors and eight had myopic errors.

Four cases having greater than three diopters of residual accommodation are listed as failures in Table 3.

TABLE 1

AGE DISTRIBUTION OF SATISFACTORY CASES

Years	No. Patients
9 to 11	4
11 to 16	11
16 to 21	2
21 to 26	3
26 to 30	1

COMMENTS

It is believed that satisfactory cycloplegia for refraction with homatropine can be produced in most patients with a single instillation of solution. The solution with phenylephrine seems to produce slightly greater cycloplegia and the eyes show less irritation as judged by the white appearance. Cycloplegia is greater 90 minutes following instillation than after 45 minutes.

TABLE 2

RESIDUAL ACCOMMODATION AVERAGES OF THE SATISFACTORY CASES

Minutes after Instillation	Number of Patients	Residual Accommodation (diopters)	
		Homatropine and Phenylephrine	Homatropine
45	15	2.0	2.2
60	21	1.8	2.1
90	21	1.7	1.9

* From the Marquette University Eye Clinic, F. Herbert Haessler, M.D., Director.

† Methyl cellulose (4,000-centipoise) 0.225 produces a less viscid solution which has been used for refractions but has not been evaluated.

TABLE 3

FAILURES

Age (years)	Refractive Error	Pupil Dilatation	Residual Accommodation (diopters)		Cause of Failure
			Homatropine & Phenylephrine	Homatropine	
12	myopia	both-wide	4.3	4.3	Unknown
13	myopia	both-wide	3.4	3.4	Unknown
15	myopia	both-wide	4.4	6.0	Unknown
28	hyperopia	O.D.—mod. O.S.—slight	3.6	7.7	Excessive tearing

SUMMARY

1. Methyl cellulose with homatropine and with homatropine and phenylephrine solutions was used in a single instillation to produce cycloplegia for refraction.

2. Residual accommodation was measured in 25 cases; four cases were found to have unsatisfactory cycloplegia.

3. The methyl cellulose solution with homatropine and phenylephrine seemed to produce slightly greater cycloplegia than the solution without the phenylephrine.

1684 North Prospect Avenue (2).

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AN IRIS RETRACTOR AND EXPRESSOR*

FOR ROUND-PUPIL INTRACAPSULAR CATARACT EXTRACTION

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Brooklyn, New York

The handling of the iris is of paramount importance in properly executing the round-pupil intracapsular cataract extraction. An instrument* was devised for this particular purpose and especially for those cases in which the pupil is partially constricted or remains somewhat rigid.

It functions efficiently as an iris retractor and opens the pupil wide, simulating the conditions ordinarily achieved by complete iridectomy. When the retractor is in place it facilitates grasping the superior pole of the lens in performing the round-pupil sliding method of cataract extraction. It is also used as a lens expressor in the tumbling method of extraction.

The instrument has a double end and can serve for other useful maneuvers in cataract surgery. However, one end is primarily used as an iris retractor and the other as a lens expressor. It measures 145 mm. in length and consists of the following parts: (1) Iris retractor: (a) right angle lip, (b) shank; (2) cylindric handle; (3) semicircular lens expressor; (4) blunt-tipped expressor and heel.

* This instrument is manufactured by Storz Instrument Company, 4570 Audubon Avenue, Saint Louis 10, Missouri.

Fig. 1 (Rizzuti). Iris retractor (A) and expressor (B) for round-pupil cataract operation.

Fig. 2 (Rizzuti). Iris retractor lip and shank elevated above line of pull of cyclindric handle.

Fig. 3 (Rizzuti). Iris retractor shank set off at a 20-degree angle from long axis of cylindric handle.

Fig. 4 (Rizzuti). Semicircular Arruga-type lens expressor. Blunt-tipped expressor and heel for "stripping of the zonule."

Use of instrument

The iris retractor consists of a short almost right-angle bent lip and shank. The lip edge is smooth and can be passed with ease under the superior border of the iris and thus obtain maximum iris retraction and dilatation.

The shank is thin and is shaped on a higher plane than the cylindric handle so that when direct pull upward is made, no backward pressure is produced to dislocate the lens into the vitreous. It is set at a 20-degree angle from the vertical so as not to interfere with direct line of vision.

With the iris retractor in place, a Verhoeff or Arruga lens forceps can then be easily applied to the superior pole of the lens for its removal. If any difficulty is encountered in grasping the superior lens capsule, as assistant can use the tip of a small muscle hook to apply pressure backward just within the lower corneal limbus to tilt the superior pole of the lens forward and hence facilitate the grasping of the capsule.

The blunt tip of the instrument is used for direct backward pressure just within the lower corneal sulcus to break the zonular fibers prior to lens extraction. It is also used as an expressor and for counterpoint pressure at the inferior corneal limbus opposite the line of traction in the sliding method of cataract extraction.

In selected cases, the heel of the expressor can be used superiorly "to strip the zonule" in the manner advocated by Kirby. When a corneal suture is used to elevate the corneal flap for better visualization, the suture can be easily engaged with the inside of the heel of the instrument at the completion of the operation. This will approximate the wound edges and forestall any possible vitreous loss.

The semicircular lens expressor is of a modified Arruga type and is particularly useful in cases of intumescent cataracts where the suction cup is applied with the use of the tumbling technique. It supports the lens and tucks the cornea under the inferior pole of the lens which affords great protection to the vitreous.

The light-weight, knurled cylindric handle lends itself to easy manipulation between the fingers and it can be quickly flipped over during the operation when indicated, so that either end can be used for its particular purpose.

160 Henry Street (1).

EYE-DRESSING TRAY

RALPH J. CARBO, JR., M.D.
Washington, D.C.

A small eye-dressing tray for hospital or office use, especially in hospitals where ophthalmology is a surgical subspeciality, is very useful. This small well-equipped portable tray can be kept sterile and up to date in central supply, ready for instant use.

The overall dimensions are 7.5 by 12 by 7 inches high. It is made of 0.5-inch plywood. The base board is 9 by 13.5 inches, allowing a 0.75-inch border for the 16 0.25-oz. bottles to set on, surrounding the tray. To the sides, two inches high, are stapled loops of elastic binding tape to hold the dropper bottles in place. The top is 7.5 by 12 inches, divided into three sections: the middle having two equal compartments for ointments, loupe, penlight, eye patches; the two side sections have cutouts for holding jars—on one side, a pound jar for sterile flats and a 4.0-oz. short jar for applicators; on the other side a Zeigler wash bottle and a 6.0 oz. bottle for sterilizing instruments.

Fig. 1 (Carbo). Eye-dressing tray.

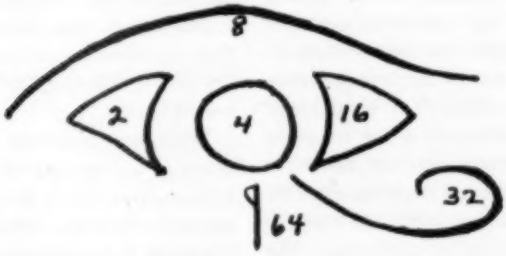
The 16 dropper bottles are usually sufficient for standard prescriptions as well as the doctor's favorite preparations. Not only are the bottles labelled but also their places on the tray, so if any medication is missing, it can be readily replaced.

The tape dispenser is mounted on the outside, thus completing the tray.

1746 K Street, N.W. (6).

OPHTHALMIC MINIATURE

The Eye of Horus



The hekat was an official corn measure in ancient Egypt and its submultiples, ½ to 1/64, were written always in symbols now known as Horus-eye notation—since these symbols can be arranged to form a conventionalized outline of a human eye. Their separate use as fragments causes the reference to Horus as in the story that one eye of his was torn to pieces in the fight with Seth.

Condensed from A. E. Berriman:
Historical Metrology, 1953, pp. 91-92

SOCIETY PROCEEDINGS

Edited by Donald J. Lyle, M.D.

COLLEGE OF PHYSICIANS OF PHILADELPHIA

Section on Ophthalmology

March 19, 1953

Dr. George F. J. Kelly, *chairman*

Bilateral metastatic carcinoma

Dr. Carroll R. Mullen, Dr. Perce DeLong, and (by invitation) Dr. Charles G. Steinmetz, III, said that metastatic carcinoma of uveal tract was first reported in 1872. A review in 1936 found 229 cases, of which 156 were histologically verified, and the binocular involvement was about 20.8 percent. The occurrence in clinical patients varies from 1 in 30,000 to 1 in 150,000. It is the most frequently encountered secondary tumor of the eye, and is believed to be more frequent than the literature indicates.

The primary site in women is the breast and in men the lungs. This incidence is not consistent with the incidence of the primary tumor throughout the body, but is influenced by the viability and the ability of the cells to implant after they have metastasized. Anatomic directness of the arteries is responsible for the involvement of the left eye more frequently than the right. The most usual site of choroidal metastasis is the temporal side of the posterior pole near the macula.

Histologically, the tumor depends upon the nature of the primary growth and may be medullary, scirrhus, or adenomatous. The tumor cells spread from their metastatic site in the lines of least resistance along the lymph spaces and between the planes of the choroidal stroma.

Treatment in these cases is palliative. Radiation to the globe does inhibit the spread and maintains useful vision to the end.

Miss B., a 56-year-old white woman, was seen in the office of Dr. Mullen with chief complaint of bilateral diminution of vision starting three months after a right radical mastectomy. Extensive involvment of the axilla was noted at surgery. Radioactive-phosphorus studies were positive in both eyes with a 120 percent, O.D., and 110 percent, O.S., variation from mean.

Roentgen examination of the chest showed rapidly extending metastatic involvement. Postmortem examination disclosed extensive metastatic lesions in all the organs. The globes were sectioned with the orbital contents. The left eye showed a flat choroidal tumor involving the entire posterior segment. The retina was completely detached. In the right eye, the picture was similar with extensive involvement and detachment. However, the anterior segment was involved, especially the ciliary body, with tumor cells breaking into the anterior chamber at the angle. The tumor cells were slightly differentiated with suggestion of acinar formation and mitotic figures. Neoplastic emboli were found in the vessels of the retrobulbar tissue and extraocular muscles of both eyes.

Discussion. Dr. Perce DeLong: Metastatic carcinoma is the most common secondary tumor affecting the inner eye; nevertheless, it is rare.

Metastasis is usually blood-borne and, because of the number of short ciliary arteries (about 20), this is the most frequent route through which the emboli enter the inner eye. The site of the growth is also important because of the distribution of these vessels; the metastatic expression is usually on the temporal side and in the region of the macula.

Metastatic lesions of the anterior segment are rare; 17 microscopically proven cases have been reported. In these cases the emboli have been carried by one of the two long ciliary arteries.

Iris involvement is extremely rare and usually occurs as an extension from the limbus. Bilateral metastatic carcinoma of the choroid has been recorded in the literature only four times. Metastatic extensions to the orbit are also rare; Reese in his textbook, *Tumors of the Eye*, reports only 19 proven cases.

In each globe of the case here presented, there are three separate lesions; each one is the result of an implanted embolus. Two lesions in the right eye resulted from emboli entering through a short ciliary artery. The third lesion at the base of the iris and ciliary body is the result of an embolus entering through a long ciliary artery. It is regrettable that a gonioscopic examination was not made to determine if this neoplasm could have been observed. In the left globe, all three lesions must have resulted from emboli entering through the short ciliary arteries.

Metastatic carcinoma of the eye is more frequent than statistics show. These metastatic expressions appear in the late stages of the disease. The patient usually is not ambulatory, is debilitated and seldom is cognizant of his visual impairment.

Furthermore, if an ophthalmologist should visit a cancer ward, he would usually find several solid detachments which in all probability are metastatic lesions.

Beta radiation using the strontium-90 applicator

Dr. William F. Hughes, Jr., Chicago, the guest speaker, said that, in the past relatively few clinics have had radon available as a source of beta particles for the treatment of certain superficial conditions of the eye.

Now that radium D-E and strontium-90 applicators are commercially available to a larger number of physicians, it becomes more important that the ophthalmologist be aware of the rationale, indications, contraindications, dosages, and dangers of beta therapy. I will attempt to: (1) Re-evaluate the results we have had in over 235 eyes during the past four years at the University of Illinois, using a radon application previously described (Tr. Am. Ophth. Soc., **50**:469, 1952), especially in regard to the selection of cases and undesirable reactions; and (2) present the preliminary results and certain disturbing problems of the new strontium-90 applicator manufactured by Tracerlab. This portion of the work was done by Dr. Fred M. Wilson, Indianapolis, and Dr. James E. McDonald, Chicago. In any new applicator it is necessary to know the physical characteristics, quality, and quantity of output.

The general dosages of contact therapy used with the radon applicator are as follows:

1 gm. sec.—Inflammatory conditions
2 to 3 gm. sec.—Initial doses, very sensitive lesions, and in children
4 to 5 gm. sec.—Deep corneal vascularization, limbal tumors, and vernal catarrh

By comparison of the effect on the rabbit cornea of our radon applicator and a strontium-90 applicator which was recently restandardized by Tracerlab using a vanishing-ion chamber, a very rough approximation of the rep output of our radon applicator would be 2,000 rep per gm. sec. ($\pm$50 percent). Treatments are given every three to eight weeks; in general longer spacing and smaller doses are now used.

Usually, the indications for beta therapy are the same as those for other radiation therapy, such as X-ray or gamma radiation. The tissue to be destroyed must be more sensitive to radiation than the surrounding normal tissue. With extremely low doses, inflammatory conditions are apparently benefited. An indication for beta-radiation therapy should imply that this therapy is not only effective but is superior to other methods of treatment because of the still somewhat uncertain effects of radiation therapy on the eye:

Indications for beta therapy

Treatment of choice
Epithelial tumors of limbus and cornea

Vernal catarrh, palpebral or bulbar forms associated with severe symptoms
Vascularization complicating keratectomy and keratoplasty
Rosacea keratitis
Primary vascularizing keratitis
Recurrent pterygium (after secondary excision)
Favorable results (low doses)
Allergic and phlyctenular keratitis
Papillomas and hemangiomas of conjunctiva
Nodular episcleritis
Granulation tissue
Uncertain results
Stromal herpes simplex (low doses)
Basal-cell carcinoma of lid margin
Chemical burns (not recent)
Tuberculous sclerokeratitis
Interstitial keratitis
Trachoma, Stage IV
Salzmann's dystrophy of cornea with vascularization
Lipoidal dystrophy of cornea with vascularization
Old vascularized corneal scars
Not indicated because of undesirable features, better treatment available or no effect
Primary treatment of pterygium
Corneal scars without vascularization
Fuchs' endothelial-epithelial dystrophy
Epithelial downgrowth into anterior chamber
Acute chemical burns
Large doses for inflammatory lesions
Cicatrizing conjunctival disease (pemphigus)
Nevi
Pinguecula
Tumors of lid margin

The complications which have attended beta therapy in some of these cases include:

1. Irritability of the eye lasting more than two weeks but eventually clearing entirely (10 percent of cases), following a dosage rate of 1.0 gm. sec. or more per week with a minimum total dosage of 15 gm. sec. applied anywhere on the surface of the globe.

2. Postradiational vessels and telangiectases which may develop one to three years after treatment with doses as low as 5.0 gm. sec. in one area.

3. Epilation of the lashes which can be produced by a dose of 4.0 to 6.0 gm. sec.

4. Deep corneal ulceration when there is pre-existing ulceration or infection and excessively large doses have been applied directly over the area. This did not occur in our series.

5. Epidermalization of the conjunctiva only when beta was used for epilation, the epidermis of the skin apparently overgrowing the conjunctival surface in the treated area.

6. Glaucoma which might be expected to be a complication of beta radiation therapy which produces ischemia of the limbal region. However, the diagnosis of glaucoma is difficult in cases of advanced keratitis because tonometric readings are unsatisfactory and associated conditions, such as iritis, can produce a secondary glaucoma independent of the beta-radiation therapy. Glaucoma was suspected in seven eyes in which the total dose over the entire limbal region averaged 53 gm. sec.

7. The possibility of cataract formation following large doses of beta radiation has not been reported until recently:

In two eyes with severe primary vascularizing keratitis, 44 to 51 gm. sec. in 16 to 18 weeks over the cornea and limbus resulted in cataract formation two and one-half to three years later. Two of these cataracts became rapidly intumescent and were extracted uneventfully except that the somewhat retarded healing of the corneal incision resulted in a filtering bleb. The other eye in one of these patients received 39 gm. sec. within 34 weeks, and a posterior subcapsular cataract developed after approximately four years. This has not progressed during the past six months, vision remaining about 20/70.

Two eyes with recurrent pterygium were treated with total doses of 28 gm. sec. over a period of months, and were found upon wide dilatation of the pupil two to three years later to have small sector-shaped areas of vacuolization in the region of the equator of the lens beneath the area of treatment. These opacities are not detectable clinically through the undilated pupil.

Due to the uncertainty of the rep output of the applicator and some variability in the reported depth doses (namely, 2 to 11 percent at 3 mm., 1 to 7 percent at 4 mm., and 0.8 percent at 5 mm.), the amount of beta and gam-

ma radiation reaching the lens (average distance of anterior capsule of lens being about 3.5 mm. from surface of limbus and 4.0 mm. from surface of cornea) can only be estimated roughly.

In the cases of primary vascularizing keratitis just mentioned, which developed cataracts, perhaps 800 to 3,200 rep reached the lens. In the two cases of recurrent pterygium in which radon was applied only in one area directly over the limbus and therefore only 3.5 mm. from the equator of the lens, where the "lens bow" of epithelium is located, perhaps 560 to 2,240 rep reached the lens.

The new radioactive strontium-90-yttrium-90 beta applicator first reported by Friedell, Thomas, and Krohmer in 1950, and studied by Wilson and McDonald, has several virtues —long half-life of 20 years, relatively low cost, high output (40 to 100 rep per sec) of pure beta particles of maximal energy 2.16 Mev (slightly less than radon), and average energy of 0.8 Mev (slightly more than radon) with depth doses comparable to radon.

Its disadvantages include—large size with an active surface 7.8 mm. in diameter, uncertainty about evenness of layering of the Sr^{90}, and apparent technical difficulties in measuring the rep output by means of the vanishing-ion chamber.

Three applicators which have been restandardized after one or two years have shown an apparent drop in rep output of 33 percent. Until the physical method of measuring the surface output of these applicators becomes consistent, it is mandatory that each applicator be standardized on a rabbit cornea.

Wilson has termed the dosage necessary to produce a definite nebular opacity on the rabbit cornea which persists for two to three months the "minimal inflammatory dose." With the change in physical measurements of the rep output, the minimal inflammatory dose has decreased from 36,000 rep to 20,000 rep. The clinical dose necessary to eliminate superficial corneal vascularization in humans is approximately 8,000 rep (0.4 minimal inflammatory dose) according to the latest standardizations, and the skin erythema dose is about 1,400 rep (Wilson).

The clinical results with the Sr^{90} applicator, using these doses, are comparable to those obtained from radon. In flat preparations of rabbit lenses, Wilson has found nuclear pyknosis, fragmentation, and balloon cells in some of the epithelial cells 100 days after exposure to 1.7 minimal inflammatory dose (34,000 rep). No clinical signs of cataract were present, and this does not represent a threshold dose.

What is a safe noncataractogenic dose of beta radiation? Unfortunately, such data are not available even for X-ray and gamma emanations whose ionization can be measured accurately. Cataracts can be produced in rabbits with X-ray doses as low as 200 r, but have not been reported in humans with divided doses totalling 400 r, and can, but not necessarily, be produced by 1,000 r.

Assuming that 400 r is noncataractogenic and that X rays can be approximately equilibrated with beta rays, a depth dose of 5.0 percent at 4.0 mm. using beta would indicate a noncataractogenic dose of only 8,000 rep of beta applied to the surface of the cornea. It is probable that this dose is unduly low because:

1. The reported rep output of the beta applicators may still be unduly high on an absolute basis which could be compared to the ionization produced by X rays.

2. The entire lens is not exposed after treatment with small beta applicators, so the safe dose may be 8,000 rep in any one area.

3. The possibilities exist that histologic changes in the lens epithelium can take place without cataract formation, that recoverability is possible, or that opacities may remain localized and nonprogressive.

In conclusion, the question probably arises: Is beta radiation too dangerous to use on the eye?

Beta radiation, especially with the new

Sr^{90} applicator, should still be considered experimental. A more consistent physical measurement of output is needed so that clinical dosages can be standardized and more accurate depth doses be obtained. Beta radiation should be used only in specific cases in which it has a good rationale and is superior to all other methods of treatment. Minimal doses and more protracted intervals between treatments should be employed.

A calculated risk of cataract is present if a total dose of over 10 gm. sec. of radon is given in any one quadrant and more than 30 gm. sec. over the entire globe with a radon applicator of our size, and an estimated 16,000 rep in one area with the Sr^{90} applicator.

M. Luther Kauffman,
Clerk.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

March 2, 1953

Dr. Abraham L. Kornzweig, *president*

Three new cycloplegic drugs

Dr. Bernard C. Gettes said that three new parasympathetic blocking agents were tested clinically, and their use in 0.5-percent solutions was previously reported. These compounds are esters of disubstituted acetic acids, and are known as Compounds GT-75 (Cyclogyl), GT-92, and GT-93. This report concerns their use in one-percent solutions.

Over 100 Negro patients were refracted with each of these drugs. The depth of cycloplegia compared favorably with the results seen after using one-percent atropine-sulfate solution as drops. For adult white patients, one instillation of any of these solutions will produce adequate cycloplegia within one hour. In children, the instillation should be repeated in five minutes. Negro patients should, likewise, have two instillations.

Duration of cyclopegia. Over 90 percent of the patients refracted were able to read eight hours after the instillation of the drops. In 40 percent of those tested, mydriasis persisted for 24 hours, in the absence of cycloplegia.

Therapeutic use. These drugs were also used to treat cases that had previously exhibited local reactions to both atropine and scopolamine. Both cycloplegia and mydriasis were adequately maintained if the drops were repeated every three to four hours. No patients exhibited any local or systemic toxic reactions to these preparations.

Conclusions. Compounds GT-75, GT-92, and GT-93 in one-percent solutions are more effective for refraction than the currently used shorter-acting cycloplegic drugs. These solutions leave as little residual accommodation as atropine. Since their cycloplegic effect is of such short duration, the chief handicap of maximum cycloplegia, namely, the prolonged blurring such as is obtained after atropine, is obviated. These drugs do not appear to produce any local or systemic effects. It is further recommended that atropine be used for refraction only in preschool children with some existing muscle anomaly; for treatments only when frequent instillation (many times a day) of drops is not desired.

Discussion. Dr. Priestley said that he had very little to add to this paper. He has been using Compound GT-75 for about two years and has had no cases of allergy. He has found that his patients recover completely in one day from the effects of the drug. He said that he uses 0.5-percent solution because he found the one-percent solution to be too irritating. He has never had occasion to try this drug on Negroes. He has found it unsatisfactory only in squint cases.

Dr. Pascal remarked that the subjective method of measuring the residual accommodation as outlined by Dr. Gettes is not satisfactory for several reasons. There is a

strong positive spheric aberration along the margin of the dilated pupil which partly vitiates the results. When dealing with small children, the test is uncertain.

A far better method of testing for and measuring the residual accommodation is by means of dynamic retinoscopy. It is an objective method, is rapid, and can be done at intervals to test the depth of cycloplegia. Dr. Pascal added that the method of dynamic retinoscopy can be used for several purposes in refraction. Ophthalmologists, by not taking kindly to the method, are depriving themselves of a valuable technique for measuring residual accommodation.

Dr. Ehrlich said that, in general, he found the same results as Dr. Gettes. He found that one drop of one-percent solution resulted in at least as efficient cycloplegia as two drops of 0.5 percent. Analysis of the depth of cycloplegia after 30 and 60 minutes showed an equal degree of residual accommodation at both times in half of the subjects, while a somewhat greater degree of residual accommodation was found at the end of 30 minutes in 25 percent of the subjects, with the reverse being the case in the remaining 25 percent, indicating that satisfactory cycloplegia is present 45 minutes after instillation. The eyes of Negroes did not show consistently satisfactory cycloplegia with one drop of one-percent solution of Compound GT-75, but did when a second drop was instilled 10 minutes after the first.

Postcards with small print were given to the patients and were mailed back after the patient indicated the time he was first able to read the print. It was found that 18 percent were able to read the print in less than three hours, 68 percent could read the small print in less than five hours, while all but seven percent could read it in less than seven hours.

It was concluded that these solutions, especially Compound GT-75, which showed the briefest duration of effect, are the most desirable cycloplegics available for refraction.

Dr. Gettes thanked the discussors. He said that he agreed with Dr. Pascal and the only reason that he did not use dynamic retinoscopy was because he was not aware of it at the beginning of his studies and, in order to be consistent, he could not introduce a new method in the middle of his work.

He said that 0.5-percent solution is effective in 74 percent of the cases tried. The stronger solution is effective almost 100 percent of the time. Therefore, Dr. Gettes said, he used the stronger solution since there is no sense in having a cycloplegic which is not always effective.

To Dr. Ehrlich he said that the idea of having the patient fill in and return a postcard is not too reliable and depends on how the postcard is worded. He said that he keeps his patients at the hospital and usually, by the end of six hours, most of the effects of the drug have worn off.

Uveitis following cataract extraction

Dr. Bernard Kronenberg presented a paper on a form of uveitis which occurs in the unoperated eye following cataract extraction in the fellow eye. This clinical entity must be differentiated from sympathetic ophthalmia and a coincidental uveitis. Dr. Kronenberg discussed the clinical concept of anophthalmitis anaphylactia. He presented four cases of this type of uveitis. He believes that this condition is really bilateral and that these patients probably first have a fleeting attack of iritis in the operated eye. It is likely that a rupture of the lens capsule in the second eye initiates the uveitis.

The most important feature of this presentation was that Dr. Kronenberg advised the prompt removal of the lens in the second eye, even in the presence of inflammation. He stated that nonintervention leads to total loss of the eye. He emphasized the fact that at no time does the eye first operated show any inflammation.

Discussion. Dr. Gartner said that he was very glad that Dr. Kronenberg had described

this process which has never been published as a separate entity.

Dr. Gartner said that he had a patient, a 63-year-old man, with arrested tuberculosis, who was anxious to avoid an operation for cataract. Only after he developed mature cataracts in both eyes did he consent to be operated. The right eye was operated extracapsularly; recovery was uneventful until six weeks postoperatively when the patient developed uveitis of the left eye. This uveitis became intractable and the patient developed secondary glaucoma and the eye was enucleated.

Section of the enucleated eye showed a granulomatous uveitis with infiltration into the optic nerve. Dr. Yudkin had enucleated two eyes under similar circumstances. Slides also showed a granulomatous type of uveitis with infiltration similar to Dr. Gartner's and Dr. Kronenberg's cases.

Dr. Gartner said that this type of case has been discussed many times in the literature. Haik describes a case of cataract extraction with uveitis and secondary glaucoma. The patient also had uveitis and secondary glaucoma in the second eye. The question was whether this was sympathetic ophthalmia or uveitis. He took the chance and removed the cataract in the second eye. The uveitis and glaucoma persisted.

Dr. Gartner said that he saw a number of cases at the New York Eye and Ear Infirmary with bilateral uveitis. Sections of these eyes showed a granulomatous type of uveitis in several of the cases and not sympathetic ophthalmia.

Dr. Berliner congratulated Dr. Kronenberg on his presentation. He said that the main question is how this inflammation starts in the second eye. He said that, in a lens which had become intumescent, he saw tiny flakes of lens matter floating in the aqueous. Was this due to a spontaneous rupture of the capsule? It is not possible to eliminate rupture of the posterior capsule. In a cataractous lens there may be liquefied soft lens matter which ruptures into the eye. He said that the intracapsular cataract operation is still preferable to the extracapsular extraction.

Dr. Agatston said that it is remarkable that this entity should be brought to our attention in this age of the intracapsular operation. Is this syndrome more common than it used to be? He asked Dr. Kronenberg if he had any experience with skin testing with lens antigen. He also asked whether the cortisone was used locally, orally, or by injection. Do these patients have a general history of allergy?

Dr. Friedman asked whether Dr. Kronenberg would remove the second lens if it were clear.

Dr. Kornzweig described two cases he had. One was that of a 78-year-old woman, operated by another doctor, who had bilateral uveitis. The unoperated eye developed secondary glaucoma, was removed, and found to have a nonspecific granulomatous uveitis —not sympathetic ophthalmia. The patient developed good vision in the operated eye. The second case was that of a 78-year-old woman, with a mature cataract of the right eye. Intracapsular cataract extraction was performed and several months later the patient developed uveitis of the other eye. The eye was removed and the operated eye never developed any inflammatory reaction. The enucleated eye showed on examination a nonspecific uveitis.

Dr. Kronenberg replied to Dr. Gartner that, if the lens had been removed in the second eye, the result might have been good.

To Dr. Agatston he said: It happens, even to the best of us, that, without intention, we have an extracapsular extraction. Perhaps we are now better able to diagnose this condition correctly. Skin testing has been done with lens protein. Cortisone has been used locally in two cases. History of allergy was found in two cases; whether the other patients had an allergic background is not known.

To Dr. Friedman, Dr. Kronenberg said that he hasn't had this experience so far. In all his cases, a cataract developed in the second eye.

To Dr. Kornzweig, Dr. Kronenberg said that it is interesting that Dr. Kornzweig had one patient who developed uveitis after an intracapsular operation. It's possible that a small amount of lens substance had escaped during the operation.

Migraine and tension headaches

Dr. Arnold P. Friedman said that the two most common headaches that confront the physician are migraine and tension headaches. In recent years, new data, made available through experimental and clinical investigation, have given the physician a better understanding of the diagnosis and treatment of tension and migraine headache. The present purpose is to summarize these problems in the light of certain recent advances and of observations on 2,000 patients during the past seven years.

Although migraine probably has many causes, it represents a definite clinical entity and has a common underlying mechanism. It is a syndrome in which the outstanding feature is periodic unilateral headache, usually associated with gastro-intestinal symptoms and often preceded by visual or psychologic disturbances. There is frequently a history of similar headaches in the parents or other members of the family. Tension headache has a more specific etiology but is not as precisely defined clinically or physiologically. This type has no premonitory symptoms, is usually bilateral, occipital, or frontal, and may be accompanied by a variety of associated signs including anxiety, nausea, and vomiting.

It has been postulated that exposure to noxious stimuli of sufficient or prolonged intensity results in the inability of the body to adapt to stress which, in turn, causes certain vasomotor changes in the cranial circulation producing cranial pain.

The mechanism by which the nervous and hormonal systems function in producing these physiologic changes is but partially understood. It would appear that the neural mechanism operates directly upon the vasomotor system via the hypothalamus and sympathetic nerves; while the hormonal system operates indirectly and is dependent upon a previous activity of the anterior lobe of the pituitary, which is stimulated by epinephrine released from the adrenal medulla and by certain substances produced locally in the hypothalamus. This activation of the anterior pituitary produces an outpouring of ACTH which results in stimulation of the adrenal cortex and produces further metabolic and electrolyte changes in the cranial circulation.

In migraine, the immediate cause of pain is associated with dilatation of cranial arteries. A similar situation exists for tension headaches except that primary or concomitant muscular spasm of the skeletal muscles of head and neck is a more important component.

In patients with migraine and tension headaches, a variety of psychogenic factors have been related to the headache. Attempts have been made to relate specific personality patterns to migraine and to tension headaches. In my experience the personality manifestations in these people are extremely variable and may include a variety of emotional factors. Most of these are unconscious and include hostility, identification with a family figure, a wish to remain in a position of dependency, or a means to gain love, affection, or attention.

In comparing migraine and tension headaches, certain clinical features appear to be characteristic of each, although there are wide variations in each group and the same individual may have both types of headaches.

The outstanding feature of migraine is the periodic throbbing headache which is unilateral in three out of four patients and,

in over half, occurs in the supraorbital frontal region. Prodromal symptoms are present in three out of four patients and are of considerable variety including visual disorders, gastro-intestinal irregularities, disturbances of the psyche and the autonomic nervous system. During the headache phase, a majority of patients are in considerable distress and frequently complain of nausea, vomiting, emotional disturbances, photophobia, and disturbances of the autonomic nervous system.

In two thirds of the patients, the onset of headaches occurs before 20 years of age. Most patients are females and a family history of migraine is frequently present. Daily headaches are most unusual and the duration of the headache is usually less than three days.

Tension headaches also occur predominantly in females but are bilateral in nine out of 10 cases and constant or daily in over half of the patients. Their clinical features show wide variations and the individual in whom the attacks are stereotype is rare. Premonitory symptoms are rarely present in the tension group. (This lack of preheadache phenomena was quite striking in our patients.) The majority of patients with tension headache date the onset in the second decade and describe their pain as "dull," "throbbing," or "pressure." Associated symptoms are common accompaniments of the tension headache, but are extremely variable and not as severe as in migraine. Anxiety, depression, nausea, and photophobia are frequently noted.

In the treatment of migraine and tension headaches a variety of methods have been used and analyzed in our Headache Clinic for the past seven years. It has been our experience that a dual approach—pharmacotherapy and psychotherapy—is the most successful method of treating both types.

Symptomatic treatment of migraine is most effective by use of oral or rectal ergotamine tartrate and caffeine (Cafergot). Symptomatic treatment of tension headache is best accomplished by use of analgesic and sedative combination (Fiorinal). Psychotherapy is the most effective prophylactic measure in treatment of migraine and tension headache.

Discussion. Dr. Knapp said that he has seen a number of patients with headaches, who have astigmatism. Refraction with atropine and correction of the astigmatism often cures the headaches. Several of these patients report a return of the headaches when new correction is needed.

Dr. Chamlin said that an extensive study was made at the Montefiore Hospital of headache patients. He said that there were practically no cases of refractive errors resulting in headaches. Photophobia was a very prominent symptom. This is not a simple observation, often the visual symptoms are lumped together. The patients often have burning and photophobia. True scotomas are rare; instead, the patients have scintillating scotomas. In cases with real field defects, brain tumors or vascular anomalies are usually present. If there is a persistent field defect, it is not a true case of migraine.

Dr. Friedman concluded by saying that Dr. Chamlin had answered the questions. Routinely, every patient has an eye examination. He said he was never very impressed by the idea that refractive errors cause migraine. Migraine is not a syndrome of only one origin, it has multiple etiologies.

Bernard Kronenberg,
Recording Secretary.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

412th meeting—March 18, 1953

DR. ANDREW L. MACMILLAN, JR., *presiding*

DIABETIC RETINOPATHY

DR. JONAS S. FRIEDENWALD, speaker of the evening, reviewed the concept of capillary aneurysms and their relationship to the Kimmelstiel nodules often found in the kidneys of diabetics.

Clinical and experimental reports were cited indicating that many diabetics have increased adrenal activity, which may cause the microaneurysms in the retina and Kimmelstiel nodules in the kidneys. Adrenal cortical adenomas were found in two percent of nondiabetics and in eight percent of diabetics. About three percent of diabetics without Kimmelstiel kidneys had adrenal cortical adenomas, while 14 percent of the Kimmelstiel cases had adenomas.

The eosinophilic response to the ACTH test devised by Thorne showed relatively more adrenal function in diabetics with retinopathy than in those without retinopathy. The Silver-Porter test showed a vastly higher concentration of adrenal steroids in the urine of diabetics with retinopathy than in normal people and in diabetics without retinopathy.

Rich found that the administration of cortisone in sizable amounts over a very brief time to normal rabbits produced lesions in the kidney that resembled Kimmelstiel nodules in 30 percent of the cases. Dr. Becker found that cortisone similarly administered to animals with alloxan-produced diabetes showed Kimmelstiel nodules in 75 percent of the cases.

A nondiabetic man who had been given heroic doses of ACTH for eight months died suddenly from a previously undiagnosed carcinoma of the bronchus. At autopsy, kidney lesions were found that looked exactly like the Kimmelstiel nodules of diabetics.

A report by Saskin was mentioned in which administration of testosterone to diabetics led to remission of retinopathy in about 50 percent of the cases. Testosterone has been shown to diminish the secretion of ACTH by the pituitary and thus diminish adrenal function.

The frequent occurrence of neuritis in diabetics and the higher incidence of retinopapthy in diabetics with neuritis suggests that vitamin deficiency may play a part in both. Experimental evidence indicates that increased adrenal function prevents the storage of vitamin B_{12} in its normal fashion and that B_{12} deficiency increases the cortisone effect on the kidney.

Having developed the hypothesis that increased adrenal secretion and vitamin B_{12} deficiency may be key factors in the development of diabetic retinopathy, a series of 24 patients with diabetic retinopathy was reported in which they were given testosterone and vitamin B_{12} for about four months. Three had exacerbations of their retinopathy in spite of treatment. Approximately half of the remainder showed no change, and the other half showed some improvement. These results were not considered conclusive.

Discussion. DR. HOWARD F. ROOT: I think everyone here will sympathize with me as I quote from the chapter in Isaiah in which the Lord gave some consolation by saying: "Fear not, thou worm." Anyone who undertakes to discuss a paper by Dr. Friedenwald needs to know not only what he has said, but all of internal medicine. Needless to say, it is always a privilege to hear Dr. Friedenwald present the results of his investigations in the field of diabetic retinopathy; and we of the New England Diabetes Association are conscious of our indebtedness to him and to the New England Ophthalmological Society which has made this occasion possible.

The close association between the retinal aneurysms and the glomerular nodules described by Kimmelstiel and the ultimate de-

velopment of arteriosclerosis, hypertension, and renal failure in the diabetic patient is today our greatest problem—especially in the severe diabetes which has its onset early in life. Indeed, the problem of blindness and these kidney lesions has become so great that I would like to call your attention to the fact that on the listings for the Massachusetts Commission for the Blind, the number of diabetics increased eight times between 1946 and 1951.

Furthermore, in a follow-up of our young diabetic patients who have had diabetes 20 years or more, retinal lesions in some stage, including early as well as late stages, were present in more than 80 percent. This problem is of such importance that it should soon become a major element in the problem of the invalidism due to diabetes.

The striking experimental evidence which Dr. Friedenwald has brought forward of the possible relationship between the diabetic state and the adrenal cortical hormones is of fascinating interest. He has already commented upon the fact that many clinical studies have indicated that the ordinary diabetic patient probably shows more evidence of underfunction than of overfunction; but there remains the interesting fact that in the uncontrolled diabetic, particularly the diabetic who has had diabetic ketosis, it has been demonstrated on more than one occasion that there is an outpouring of cortical hormones and that emergency—the emergency of diabetes uncontrolled—is the factor which underlies and is present in the majority of these diabetic patients. That factor has been used as an interpretation, as a means of explaining the fact that pulmonary tuberculosis occurs with such extraordinary frequency in the diabetic patient who has had ketosis. Cortisone is well known experimentally, somehow, in some way, to further the development of active tuberculosis in lesions, even of the throat as well as others.

Now, the use of the new stains, especially the stains of the Hotchkiss-McManus variety, and the others, certainly has suggested that the hyalin material in glomeruli, thickened retinal aneurysms, and arterioles, is a polysaccharide—probably of the mucopolysaccharide type. Studies upon the mucoproteins of the blood have been carried out, and it seems possible to predict that disturbances in this field can be demonstrated in the blood of diabetic patients as well as in the tissues at autopsy.

Recently, new staining methods reported by Rinehart and others led them to the conclusion that the basement membrane in the kidney glomerulus is a differentiated cytoplasmic product of the endothelial cell. The surface epithelial cells elaborate a cytoplasmic secretion with properties of a mucopolysaccharide or mucoprotein.

Here, then, is the beginning of a chemical explanation for these lesions which make a common pathologic process for the eye, the kidneys, the arterioles, and the hyalin material in the hyalin cells of the pancreas.

At the George F. Baker Clinic recently, Dr. Ditzel has done some really extraordinary things. He has a method by which he looks at the capillary vessels and he not only will take patients marked X, Y, and Z, and pick out for us the diabetics and nondiabetics by the changes in the capillary walls visible through this apparatus, and the sludging of the blood, but he has gone further—he will now pick out the children of diabetic mothers and differentiate them from the children of nondiabetic mothers.

There seems to be no doubt that the essential pathologic process, so far as the vascular system is concerned, is in these small vessels —capillary, arteriolar, and so on.

I would emphasize again the relationship between the severity of diabetes and its control.

When we come to talk about therapy, Dr. Friedenwald, I cannot help but refer to some clinical data here which I am sure may seem very crude to many of you. But, we have now observed some 457 patients in the last 20

years who developed retinitis proliferans; we have seen them go from the early stage to the advanced. In these 457 patients, the striking fact is that this malignant condition is frequent in those patients whose diabetes is of a severe type and, particularly, beginning early in life. Retinitis proliferans does occur in nondiabetics, and one sees it occasionally in patients whose diabetes began late in life and would be called mild; but those rare patients, those "pet patients," so to speak, stand out as one in a hundred in contrast to the great mass of young diabetic patients that we see who are now in the process of developing this malignant state.

And then treatment. Severity does count; control does count. The fact is that there are now between 40 and 50 patients who, after 25 years of diabetes, beginning in early life, having been treated carefully with insulin daily, balanced against proper diet, now, after 25 years, have the 25-year—the quarter-century—victory medal, mainly because at the end of 25 years of diabetes, beginning early in life, they still are completely free from any retinal evidence, with no evidence of retinal lesion, with no evidence of calcified vessels, and without hypertension.

Control does count, and that was true in the other group, when classified. There are 15 or 20 percent of these patients after 20 or 25 years who are free from lesions, and those are the patients whose diabetes has been controlled. Whatever may be the pathologic mechanism of vitamin B_{12} (which I can't discuss) and adrenal cortical hormones, whatever may be the intimate final mechanism, it in some way is related to hypoinsulinism and these various endocrine factors.

DR. WILLIAM P. BEETHAM: I was pleased to be asked to say a few words about this most excellent paper. All of the papers I have heard Dr. Friedenwald give are absolutely superior.

I have been very unhappy these past years when I think of the many, many thousands of diabetic patients, possibly as many as 20 thousand, that I have examined and for whom I have been able to do little or nothing. Now it looks as if we were arriving somewhere, and maybe I will be able to help some of these patients. It looks very promising. There are four or five or six questions that I should like to ask Dr. Friedenwald.

First, I would like to ask him if he feels if there is any difference between what I call a nonproliferating type of retinopathy and the proliferating type of retinopathy. Clinically, they just don't look quite alike to me. One sometimes follows the other, but you often see the nonproliferating in old people and see the proliferating type in the young people. And so they may be the same thing, but they strike me as being just a little different.

Then, I would like to pass on to the question I have been asked a good many times: Are these microaneurysms visible with the ophthalmoscope? I have made some answers of my own to that, but I would like to hear his answer.

Then, in line with that is another question: Are these microaneurysms essentially the same process as the change we see in the larger vessels in the eye? We see large veins, sometimes they are enormous and very distended, beeded, dilated, fusiform aneurysms, and so forth. Is the process the same? There is quite a difference in the size of the vessels. One is the larger vessels; and the others are, of course, the very small vessels.

Then, I would like to ask: Did he find these Kimmelstiel nodules in diabetic patients who did not show proliferating retinopathy? It has been my impression that the patients with proliferating retinopathy are the ones that end up with renal disaster, and those are the ones that pathologically have shown Kimmelstiel nodules. There must be some in his series who have not had proliferating retinopathy—and do those show these nodules in the kidney?

I accept the fact about testosterone dimin-

ishing adrenal activity, but I would like to comment adversely on Dr. Saskin's article. He reported on only 28 cases, which I consider too small a series to be significant. Twenty-one of these cases were in women, which does not represent the true male-female distribution. He divided the cases into mild, moderate, and severe—labeling a moderately severe retinopathy as one with one to five hemorrhages. In my opinion, a moderate degree of retinopathy is 200 or 300 visible hemorrhages or microaneurysms.

Is there any difference between methyl testosterone or testosterone propionate? Saskin makes a distinction in his article—one is good and the other isn't good.

And now, finally, I want you all to realize what a great big step this is in diabetic ophthalmology. I think we have different eras in diabetes; perhaps we have approached the Friedenwald era.

DR. FRANK ALLAN: When we consider the problems of diabetic retinopathy, we may talk coldly about the histologic changes and about the chemical changes in the body, but all of us have in the back of our minds the tragedy that is represented by the loss of vision in young diabetics, in diabetics who have struggled to live in spite of diabetes for 15 or 20 or 25 years, and then often in the prime of life find their hopes frustrated by loss of sight. We all have this tragedy in the back of our minds, and it gives us hope to know about the accumulation of new facts on this condition and the application of new speculations. It gives us hope that, in time, there may be a solution to this problem and the prevention of this far too common tragedy.

DR. ELLIOTT P. JOSLIN: I have just a few words to say. What a treat we have all had tonight. Here is a man who comes to us as a specialist in ophthalmology, and he talked as if he had been brought up in clinical medicine, as if he had spent years in pathology and spent other years in advanced chemistry, and then harmonizes the whole for us. I think that is wonderful, and we certainly appreciate, Dr. Friedenwald, your giving us this treat this evening.

I am sure that I speak for a great many of the doctors here when I say, if we had diabetes in our own families, we would just keep it controlled from beginning to end.

DR. F. H. VERHOEFF: I didn't expect to speak. It is a pleasure to say a few words about Dr. Friedenwald. It seems like old times to see him here. You know, as you get older, the years pass very quickly; it just seems like a few days ago when he was working in my laboratory. He was the first of the few men who worked in my laboratory to receive the degree of A.M. from Harvard. Just a few years before, they passed some kind of rule making it possible for a man to do that. There have been very few who have done it, and I'm sure he was the first.

When he was here, we recognized his great ability; and we looked forward to his doing fine work. He has more than come up to our expectations. You know from listening to him, what a fine man—a great man—he really is.

Now, in regard to his work, two questions have occurred to me. How long do the aneurysms last ordinarily and in how many treatments do they disappear? Does the treatment cause them to rupture and prevent the formation of new ones? That's a possibility, I suppose. I am curious to know; perhaps Dr. Friedenwald would have to speculate about that, just as I am.

DR. JONAS S. FRIEDENWALD: Well, I feel very much like that lowly worm Dr. Root talked about and very much overwhelmed by the kind things that have been said. I would like to say again that my contribution to this study has been somewhat removed and that perhaps the most important contributions to it, in ideas and in work, have come from Dr. Becker, who is one of the most brilliant young men with whom I have ever had the pleasure of being associated. All the other members of the team have made

their contributions. It has been my privilege to sit in on the conferences, and I have done relatively little in the development of this subject.

I would certainly agree with Dr. Root and Dr. Joslin that careful control of the diabetes is desirable; and I think that the evidence that has come from the recent publications of their clinic shows that, in juvenile diabetics, the incidence of retinopathy is greatest in those patients who have had most frequent episodes of acidosis. Whether that means that the good results in the patients without acidosis are to be attributed to the care of the physician and the morality of the patient and the bad results to the opposite in the other cases, or whether those bad results occurred in patients who had in some inherent degree an uncontrollability of their diabetes is one thing that has worried me and about which I think the statistics do not tell us very much.

I would like very much to know what Dr. Root and Dr. Joslin think as to the things that happen to these young people who have been under good control and who, during early adult life or late adolescence, become uncontrollable. Is that just psychologic revolt or is there some other metabolic change that occurs at that time that makes their diabetes less easy to control?

I think both of them will agree, however, that diabetic retinopathy and Kimmelstiel nephritis do occur in patients who have the best control that the best physicians can give. That does not mean that what we now consider perfect control is perfect control. The administration of insulin in the parenteral circulation may render the blood-sugar level normal, but may not keep the level within the portal circulation normal, where glucose and insulin normally have their first encounter. So that, even in an optimally controlled diabetic, we do not necessarily have a totally normal person; and that, I think, is perhaps the reason why these lesions occur even under good control.

As I pointed out, there are cases, extremely rare, in which the retinopathy makes its appearance very early in the diabetes; and sometimes even, there are cases—as in the case I told you about—in which the retinopathy appears before any diagnosis of diabetes can be made by the most intensive tests that can be applied.

So that, while it is undoubtedly bad for a diabetic to have lack of control of his diabetes —and I have no doubt that lack of control will exacerbate the vascular lesion that he suffers from—it seems to me we have to look beyond questions of control for the nature of the pathologic process and the biochemic disturbance that underlie this disease.

At a previous meeting where I had the fortune to talk in the presence of Dr. Root, Dr. Root made a very wise and cogent statement that it was fatuous to talk about diabetes except on the basis of hypo-insulinism, and I certainly would agree with him on that score. That is the focal point of the whole problem. But, I think also the effects of hypoinsulinism and their interaction with other metabolic disturbances in the body have to be followed through if we are to uncover the complexities of these so-called complications of diabetes.

Now, I spread out before you a lot of $64.00 questions and have a sizable number of the same sort in return. As to whether the proliferative and the nonproliferative types of retinopathy are basically different, I would say that, on the basis of the presence of capillary aneurysms, I would not think they were different—both the proliferative and the nonproliferative have aneurysms within the retina. The proliferative ones have capillary aneurysms in the proliferating blood vessels in the vitreous.

As to the question as to whether these microaneurysms are ophthalmoscopically visible: What we see under the microscope are innumerable aneurysms of an average size of 30 to 40 microns in diameter, which would be just at the limit of ophthalmoscopic

visibility if the fundus is completely clear and if they are close to the macula. However, under the microscope, we see, along with these many tiny aneurysms, a sizable number of larger ones that are up to 100 microns in diameter; and I presume it is those that we see ophthalmoscopically as the cherry spots that are characteristic of the retinopathy. I assume that every time we see one or two or 10 of those large ones, there are tenfold or maybe more than that of the small ones also present which are invisible with the ophthalmoscope.

In connection with this same question, Dr. Verhoeff asks how do these things disappear. I do not have the answer to that from any pathologic studies except, as you saw, some of them become hyalinized. They would no longer look red because there is no longer any blood in them. The hyalinized ones might still, conceivably, be visible as glassy, rounded spots, but I have never been able to see such glassy, rounded spots with the ophthalmoscope.

I did have one patient who had retinitis proliferans—a cluster of blood vessels growing out into her vitreous—and she had repeated vitreous hemorrhages. She was one of these proliferating cases. Fortunately, her vitreous hemorrhages were not very large and she would recover from them and have fairly good vision, and then get another. At times, when the fundus was clear, one could see three little cherries—looked just like a pawnbroker's sign—on the tips of the proliferating vessels sticking out into the vitreous; I was able to watch those three little cherries over a period of perhaps a year and a half—not continuously because, at times, the vitreous would become cloudy with blood. It would clear and I would be able to see the cherries again. Well, about a year after I first noticed them, they turned white and I presumed at that point they were hyalinized. Since they were sitting out in the vitreous, they could be seen as white objects, whereas if they had been in the more turbid retina they might not have been visible at all.

Dr. Beetham asked what is the relation of these lesions to the changes that we see in the larger blood vessels, and Dr. Root also emphasized the fact that, in the long run, these patients get arteriosclerosis, hypertension, and finally have widespread, complicated vascular disease. I agree that patients with diabetes, whether they have retinopathy or not, are prone to vascular disease, to arteriosclerosis, to hypertensiveness, and so on. I also agree that those with retinopathy are more prone to these complications. But, I am not at all convinced that these diseases of the larger blood vessels, which we see in diabetics both with and without retinopathy and which we see in nondiabetics, are in any direct way related to the specific vascular lesion of the capillaries.

Many years ago, I made serial sections of the eyes in a dozen cases of diabetic retinopathy in order to see whether there was any vascular disease in the larger blood vessels. Out of the dozen, half of them showed arteriosclerosis or hyalin changes—as one would expect in elderly and advanced diabetics. There were another half dozen in which, on serial section, I could discover no local vascular disease whatsoever. I feel that the capillary aneurysms, though they may be enormously exacerbated by the incidence of superimposed arteriosclerosis and hypertensive disease, are not in themselves directly the consequence of the hypertensive disease.

The same thing, I think, applies to the renal lesions; in fact, I would suggest perhaps that the progress of renal damage that occurs as the result of the Kimmelstiel lesions in the glomeruli ultimately causes hypertensive disease.

Dr. Beetham also asked whether there was any difference in the incidence of Kimmelstiel-Wilson disease in cases with or without proliferation. I haven't any statistics on that; I suspect that the incidence is somewhat higher in the presence of proliferation, but it is by no means zero in the absence. Of 70

cases with retinopathy found among 150 diabetics, I don't believe there were more than 10 that had retinitis proliferans; whereas, there was a total of 40 Kimmelstiel cases, and even if all those 10 had Kimmelstiel lesions, there would be still 30 to be accounted for. That's a rough estimate—I can't give you the exact figures.

Dr. Beetham makes, I think, some valid criticisms about the work of Saskin. I was, I confess, not very much impressed by the therapeutic argument which he advanced on a relatively small series. Early cases of diabetic retinopathy go through spontaneous remissions. We have all had our enthusiasms for one kind of treatment or another and have found that, if we put a patient on the treatment, the first time we see him, the likelihood is—if it is an early case—that he will be better three months from the first visit. So, one cannot depend on short-term observation in early cases. While I think that there may be improvements in the retinopathy as the result of the testosterone, I do not think that that has been established. I understand that the experience of a group in Philadelphia, shortly to be published, indicates that they did not have any improvement in retinopathy from testosterone.

I used the testosterone, not because it was a well-established therapeutic agent, but because there was reason to suspect that it could reduce the activity of the adrenals.

Well, I have done my best with these $64.00 questions. There are a lot of them that I certainly cannot answer satisfactorily, and I think that it would be best at this point for me to sit down.

Henry Adams Mosher,
Recorder.

Ophthalmic Miniature

We saw one hundred and sixty-four new out-patients and it was distressing to have to turn several cases away because they had come too late. I then went to the operating room and did ten cataracts "off the reel," and at about one thirty we came back to lunch—and then back again to the hospital from three to six p.m. and I did fourteen more cataract operations, twenty-four in all for the day besides sixteen other eye operations. It was the busiest day I had for a very long time, a memorable day for me—forty eye operations on what was probably my last day of ophthalmic surgery.

Sir Henry Holland (aged 78 years) at Khairpur,
Quetta Mission Hospital Report, 1953.

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TOTALITARISTIC TISSUE THERAPY

An editorial in THE JOURNAL (30:635, 1947) concluded with the following paragraph:

The danger to science of replacing the mortarboard by the pileus, the scarlet gown of the free doctor by the black shirt of Naziism or the red one of Communism, or by the star-studded hood of the necromancer, has been sadly demonstrated only too often in the past history of man's civilization. Politics and the State have no place in the premature exploitation of any medical discovery, regardless of the outcome.

We are told that following the dissolution of Charles I's third Parliament in 1629 and until the Restoration in 1660, the suspension of freedom of discussion in the English universities, especially in Cambridge, produced

a feeling of profound moral and intellectual depression. The mortar-board, a symbol of scholarship, especially that of master and doctor, was replaced, by orders of Cromwell, by a soft, brimless cap similar to the pileus of the ancient Greeks and Romans. As the devasting, dreary, and cruel days of the Puritans stretched out, forbidding freedom of expression and action, the pileus became the symbol of subservience to the State and no longer that of free scholarship. When the dreadful ordeal was over, the vice chancellor of Cambridge University, and doctors in scarlet gowns, the regents, nonregents, and bachelors with the hoods turned, and the scholars in mortar-boards (replacing the pileus) celebrated the Restoration and the return of academic freedom on May 10, 1660, with appropriate and joyful ceremonies.

This is only one example of many of the attempts of the State, in the past, to dictate the direction of men's minds, philosophies, and scientific actions. The memories of the Nazi dictation and direction of its physicians and scientists are still too fresh in our minds to be lightly forgotten, and what little we can gather from Communist Russia and her satellites indicates that the same thing is going on in those countries.

As evidence of this, an article by Prof. Leslie G. Kilborn, "Medical education in Communist China," (*Journal of Medical Education*, 29:21, 1954) is most distressingly illuminating and deserves careful emphasis.

Dr. Kilborn was formerly dean of medicine and director of the College of Medical Sciences in the West Union University, Chengtu, Szechwan, China. He had more than two years of experience under the new administration in China. He is convinced that very serious retrograde steps in China's health program are being taken. These steps involve three spheres:

1. The rejection of the traditional system of ethics which has governed the activities of the profession in most areas in which scientific medicine has prevailed.

2. The repudiation of the scientific spirit, and the substitution for it of an authoritarianism characteristic of the prescientific era.

3. The enforced lowering of standards of medical education.

It seems terribly urgent and important to include here some of Dr. Kilborn's discussion of what he means by the repudiation of the Scientific Spirit in China. He says:

> It is generally agreed that the scientist acts in harmony with what has been called the scientific spirit. By definition this includes such components as honesty in observation and in reporting results, a critical attitude as opposed to the blind acceptance of authority and the complete objectivity in the evaluation of the work of others or of oneself. All three of these components of the scientific spirit have now been condemned and discarded.

Dr. Kilborn goes on later to say:

> The insistence by the authorities of the new regime in China upon the adoption of official views in the field of science has affected medical education very directly in at least two sciences other than genetics. The first to be involved was therapeutics. This became evident in 1950 and 1951, when much publicity was given to "tissue therapy," and its adoption all over China was pushed by government agencies. . . .

The rejection of the Scientific Spirit is shown, not so much in the claims for tissue therapy, although based upon seemingly insufficiently controlled evidence, as in the insistence by official bodies that tissue therapy be adopted. A nationwide chorus of praise for the new form of treatment was raised through Communist China, both in the popular press and in professional publications:

> Nobody dared criticize the published results even though few if any attempts had been made to control properly the conditions under which these had been obtained.

Dr. Kilborn translates for us a report by Shao-Lung Ko, *Tissue Therapy*, Shanghai 1951, pages 694-695:

> The Ministry of Health of the East China Military Commission held a conference on tissue therapy, consisting of 77 persons representing each province and municipality of the area. Included were administrative officers of health, specialists and clinicians.

From August 15 to 20, 1951, they met for five days. On the final day of the conference, Vice Minister Chuen, of the East China Military Commission, reported on the findings and clearly indicated the direction to be taken in the future by the East China Area (E. C. A.) in the promotion of tissue therapy. At this conference, the E. C. A. established a unified organization for the promotion of tissue therapy, namely the E.C.A. Tissue Therapy Promotion Committee. This committee is divided into the following five sections: theoretical, clinical, productional, administrative and educational.

From the reports made by the various representatives at this conference regarding the results of tissue therapy promotion in the E. C. A., tissue therapy is being practised in 31 municipalities and counties, including 84 clinical units. Over 7,000 patients have received tissue therapy; there are reports on 5,211 of these persons. The important results are as follows:

These results are given in a table, which included 15 different diseases. The following six are typical:

Disease	No. Cases	% Showing Results
Bronchial asthma	1,077	61.3
Peptic ulcer	588	61.2
Corneal opacity	191	49.8
Optic atrophy	87	27.6
Retrobulbar neuritis	67	54.7
Corneal ulceration	49	87.8

Ophthalmologists of wide clinical experience and with a suitable knowledge of ocular pathology will look with great, and proper, skepticism at the high percentages of favorable results of this treatment in the last four diseases mentioned, particularly in optic atrophy. The colloquial Americanism, "Oh yeah?" seems to be a most suitable comment at this point.

There is no room here to discuss further the subject of tissue therapy and "biogenic stimulators" in ophthalmology. There is at hand a good review by F. Deodati (L'Année Thérapeutique en Ophtalmologie, Paris, L'Expansion, 1950, v. 1, p. 105). It is pertinent, however, to cite two of this author's conclusions. He says:

To judge by the Soviet literature, tissue therapy is really the "universal panacea," susceptible even of ameliorating chronic glaucoma, and even the healthy eye. (Sic)

In comparing their statistics with those of the Anglosaxons, one is struck by the extreme divergence of the results. Those (results) in the different statistics published by the French authors, who seem to have been more numerous in utilizing tissue therapy, are equally far from being in agreement.

In other words, apparently Communism has no room for disagreement with the therapeutic fiat of the State. You either use the methods and get results dictated from above, or else.....

Can this happen here?

Derrick Vail.

CORRESPONDENCE

Acute ocular lime burns

Editor,
American Journal of Ophthalmology:

In the February, 1954, issue of The American Journal of Ophthalmology, I read an interesting article (page 209), on "Management of acute ocular lime burns," by Walter Z. Rundles, Jr., and James R. Quinn. It is an excellent work and I sincerely congratulate its authors. In the same issue (page 270) is a report by Dr. Philip M. Lewis who also treated (Case 3) a moderately severe lime burn of the cornea and conjunctiva with cortisone.

I wish to point to the fact that I have treated many accidents due to lime burns, using, as first aid, irrigations with a concentrate of cane sugar syrup. It transforms the calcium hydroxide into calcium gluconate, harmless, noncaustic, soluble, and easy to remove from the eye.

I consider this little addition necessary. I have been using it successfully for a very long time at the Guadalajara Civil Hospital, at the Mexican Railroad Hospital, as well as in my own private practice.

(Signed) Luis Martinez, Jr., M.D.,
University of Guadalajara,
Guadalajara, Jal., Mexico.

BOOK REVIEWS

ABSTRACTS ON MILITARY AND AVIATON OHTHALMOLOGY AND VISUAL SCIENCES. By Conrad Berens, M.D., and L. B. Sheppard, M.D. Washington, D.C., The Biological Sciences Foundation, 1953. Two volumes (Volume three in preparation). Volume one, 530 pages, foreword by Maj. Gen. R. W. Bliss, Surgeon General U.S.A. (retired); Volume two, 417 pages, foreword by Maj. Gen. Malcom C. Grow (retired), formerly Surgeon General of the Air Force. Price: $20.00 per volume.

These volumes, the authors of which are well-known authorities, are the beginning of a series, composed of bibliographies and abstracts of the ophthalmic literature, of particular importance to aviation and other military services. It is, of course, natural that many other parts of the literature pertaining to general ophthalmology are included whenever there is slightest bearing upon the importance of the eye to the military problems.

Volume one covers the literature for 1940, volume two, for the years, 1941-1945, inclusive. The job is very well done.

Those interested in military ophthalmology will find these volumes a most useful tool, and every ophthalmic officer in the Armed Services should have his own desk copy for ready reference. Every library should subscribe to these volumes, too, since many ophthalmologists in civilian life will find here sources of important information on subjects that interest them.

Derrick Vail

A FURTHER STUDY OF VISUAL PERCEPTION. By M. D. Vernon, M. A. London, Cambridge University Press, 1952. Clothbound, 289 pages, 30 figures, bibliography, and index. Price: $7.00.

Miss Vernon's first opus on this subject was published in 1937 and is now out of print, as well as out of date in the light of new data in the realm of experimental psychology. The central thesis is that the sensory impulses are but the raw material from which the final percepts are constructed.

Since apprehension of form is of fundamental importance in perceiving the external world, this is studied in detail and from various points of view. The percepted environment is also related to the perceiver as its center. An individual slant, a body of personal experience, though overlaid by habit and by social custom, functions in the perceptual act although the perceiver may not be aware of it.

Perception and behavior are also affected by the length of time to which the observer is exposed to conflicting sensory data. When Stratton (1897) and Ewert (1930) wore prismatic lenses which completely inverted the visual field, the observers were first completely disorientated and could not localize objects correctly. After a time disorientation was no longer experienced and movements became more accurate. The visual field did not cease to appear inverted; but the observers had acquired a new spatial scheme in which kinesthetic impressions of upward movement corresponded to visual impressions of downward movement.

This scholarly book is essential for a more thorough insight into the problems of spatial perception.

James E. Lebensohn.

BULLETIN DE LA SOCIÉTE BELGE D' OPHTALMOLOGIE. February, 1953, Number 103, pp. 1-231. Bruxelles, Imprimerie Medicale et Scientifique, Rue de l'Orient, 67.

The Belgian Ophthalmological Society met on February 22, 1953, in Brussels. The main topic at this meeting was acquired central retinal dyschromatopsia.

The principal speaker was J. Zanen who presented this difficult subject and related clinical entities in his usual clear style and

comprehensive manner. In successive chapters he discussed the anatomy and histology of the macula, fovea and foveola, the most important facts on the physiology of this part of the retina, the theories of color perception, and studies on the pathology of the macula.

Other chapters were devoted to the methods of testing color vision, the description of an instrument newly devised by the author, the report of 43 case histories, and a discussion of several hypothetic explanations in disturbances of color perception.

A disturbance in the perception of blue indicates a central chorioretinal lesion which causes either an increase of the photochromatic interval or a reduction of the visual angle. The blue perception is very sensitive toward both of those mechanisms.

Diseases of the optic nerve or the optic pathways impair the perception of all colors. The apparent greater damage in the perception of red and yellow is explained by desaturation to which the longer wavelengths are more sensitive.

The need of further research concerning the reaction of the foveola to changes in the degree of luminosity and to the length of exposition to light was stressed. Exact color perimetry was recommended and the clinical significance of further studies in this line was emphasized.

Mlle. Watillon and R. Weekers studied the alterations of the visual fields in posttraumatic encephalopathy. Irregular contractions of the peripheral isopters and enlargement of the angioscotoma are significant. Visual-field studies should be made whenever such a complication occurs.

J. François and G. Verriest contributed an interesting paper on perimetry in reduced illumination. They reviewed the history on low-illumination perimetry, the techniques and apparatus in use, and discussed the scotopic visual fields in young emmetropes and the central scotoma in reduced illumination, as well as the outline of the blindspot and the peripheral isopters. Visual-field charts and many graphs illustrate the results achieved.

P. Daenen and R. Weekers favor the correction of high refractive errors when taking visual fields and they stressed the frequency of errors in ametropics and presbyopic subjects especially in the region 40 to 50 degrees from the macula. They demonstrated the perimeter of Goldmann with an additional support of corrective lenses. Equally good results were achieved with contact lenses. Charts of visual fields, taken with and without correction, prove the exactness of their view point.

R. Weekers and P. Daenen studied the field of fusion and the field of fixation. They charted the fusion fields for distance and near. For both purposes they used transparent red and green shields which they put over the right and left eye, respectively. The head was immobilized and the eyes followed a white target. If fusion is present, the patient only sees one gray target which occasionally appears to be rose-colored. In the superior fields even in normal persons, a heteronymous diplopia appears, caused by the physiologic divergence in elevation of the globes. In the lower field, the target appears either red or green because the nose prevents binocular perception.

For fixation fields, the authors used two different techniques. If the visual acuity was good, they used Goldmann's perimeter. If the visual acuity was poor, a transparent sphere was placed over the perimeter arc and the light reflex was registered in the extreme positions. An additional correction was necessary in adduction because of the interference of the nose. Both tests were made monocularly.

The last lecture of this excellent meeting was read by M. Appelmans, J. Weyts, and J. Vankan. They had screened the color perception in the natives of the Belgian Congo and they recorded the incidence of hereditary anomalies. They could not find any essential difference in anomalies in the white and

colored races. They evaluated their findings carefully as the number of persons examined was comparatively small and because the Ishihara plates, which were mostly used, easily cause errors in interpretation.

Alice R. Deutsch

THERAPEUTIQUES VASCULAIRES EN OPHTALMOLOGIE (Vascular Therapeutics in Ophthalmology). By Jean-Gallois. Communication to the Société d'ophtalmologie de Paris, November 16, 1952. Paris, Charles-Lavauzelle et Cie. Paperbound, 156 pages. Price: Not listed.

Jean-Gallois first presents in detail the vasoregulation of the eye and the various medical and surgical measures that may influence the ocular circulation. Then follows a comprehensive discussion of the various conditions in which vasodilation may be indicated. In diabetic retinopathy, rutin and similar agents are advised; the vasodilators may aggravate the retinal condition. Acute glaucoma may occasionally be controlled by the retrobulbar injection of alchohol and the subconjunctival injection of acetylcholine. He uses vasodilator drugs (Niacin and Priscoline) in various degenerative conditions of the retina and optic nerve and cites many instances of remarkable visual improvement: such as myopic choroiditis, from an acuity of 0.4 to 0.9; senile degeneration, from 0.2 to 0.6; optic atrophy, from 0.1 to 0.4; glaucoma simplex, from 0.5 to 0.9. Vasodilators are a valuable adjunct to other therapeutic measures. The improved circulation probably stimulates less-affected tissue to better function.

James E. Lebensohn

1954 MEDICAL PROGRESS: A REVIEW OF MEDICAL ADVANCES DURING 1953. Morris Fishbein, M.D., Editor. New York, Blakiston Company, 1954. 331 pages and index. Price: $5.00.

This volume, edited by Morris Fishbein with the collaboration of 28 contributors, is intended to relate the over-all progress of medicine during the past year with separate chapters on each specialized field. As such it is of value to the ophthalmologist chiefly in giving him a brief view of some of the recent advances in fields other than his own. A brief 10 pages are devoted to ophthalmology, contributed by M. L. Stillerman, with discussion limited to retrolental fibroplasia, the fundus in congenital heart disease, the use of cortisone and related compounds, intraocular acrylic lenses, ophthalmia neonatorum, and conservation of sight.

William A. Mann.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Alpern, M., and Faris, J. J. **Note on the electrical response of the human eye during dark adaptation.** J. Opt. Soc. Amer. **44**:74-79, Jan., 1954.

The height of the principal wave of the electroretinogram showed an increasing response with increasing dark adaptation, so that a typical dark adaptation curve could be determined. Paul W. Miles.

Bouman, M. A., and ten Doesschate, J. **Nervous and photochemical components in visual adaptation.** Ophthalmologica **126**:222-230, Oct., 1953.

Numerous previous observations by different investigators point to a nervous component in the process of visual adaptation, in addition to the well-established photochemical component. In the study under review the relationship between stimulated area and light threshold was investigated by means of light flashes of .05 second duration on retinal areas about 7 degrees nasal to the fovea. The rate of change in the amount of light necessary to produce a threshold sensation under increasing light adaptation is interpreted as another piece of evidence for a nervous factor in visual adaptation. This factor probably operates by changing the transmitting properties of the nerve elements. (6 figures, 6 references)

Peter C. Kronfeld.

Boynton, R. M., Bush, W. R., and Enoch, J. J. **Rapid changes in foveal sensitivity from direct and indirect adapting stimuli.** J. Opt. Soc. Amer. **44**:56-59, Jan., 1954.

An intense stimulus on one part of the retina reduces the sensitivity of a spatially remote area. This has been interpreted as a nervous reflex action, but experiments are presented which suggest that the loss of sensitivity is from stray light reaching the remote area to reduce contrast.

Paul W. Miles.

Brown, J. L. **Effect of different preadapting luminances on the resolution of visual detail during dark adaptation.** J. Opt. Soc. Amer. **44**:48-55, Jan., 1954.

The dark adaptation curve was produced in a modified Hecht-Shaler adaptometer with a red fixation cross, and a 35° adaptation field. Various grating test objects were used with various intensities

of five minute adaptation stimulus. With test objects requiring cone visual acuity, there was no break in the curve because under no stage of adaptation could rods discriminate the grating. Only with coarse targets could the typical dark adaptation curve be obtained. Paul W. Miles.

Giles, C. H. **The clinical testing of color-vision.** Brit. J. Phys. Optics **11**:1-7, Jan., 1954.

The Holmgren wool test has fallen into disuse, being ineffective. One must discriminate between congenital and acquired color deficiency. Tests in use for routine practice are: 1. Ishihara in daylight, 2. Stilling in daylight, 3. Giles-Archer Color Perception Unit (in darkness). Many candidates pass the two confusion tests and fail the lantern. To help children select a career at a reasonable age, it is advised that all schools make routine use of the Ishihara test, at age 13. At earlier ages, a considerably larger percentage will fail. Paul W. Miles.

Lindsay, J. **New methods in orthoptics.** Brit. J. Phys. Optics **11**:32-41, Jan., 1954.

This article begins with a review of the literature on the development of binocularity in the child. Considerable attention is given to comparative physiology in binocular animals. Some errors in present orthoptic methods include the following. Pictures are not as real and effective stimuli as solid objects which can be simultaneously handled by a child. Following an outline with a pencil is a poor substitute for fingering a solid object. Technique should include not only a sense of diplopia, but a complete grasp and consciousness of physiological diplopia. A new technique for training consists of a small table at eye level with a sagittal septum from the nose forward approximately four inches. The eyes are in such a position that the cover test can be used with loose prisms at any time during the training. On the small table before the two eyes are placed small lead animals. For instance, a rabbit is placed just beyond the septum, a bear out about 9 inches, and a cat out 12 inches. The patient is asked to handle the animals, and pay attention to physiological diplopia. Various maneuvers are described. The swan is a good test object for abnormal retinal correspondence because of its thin neck which elicits diplopia easily. The paper is quite impressive and merits attention. Paul W. Miles.

Marg, E. **Accommodative response of the eye to electrical stimulation of the ciliary ganglion in cats.** Am. J. Optometry **31**:127-136, March, 1954.

In an experimental study of the relation of accommodation in diopters to the magnitude of oscillating electrical stimulus applied to the ciliary ganglion by a pair of silver electrodes, the accommodation measured by the Rodenstock refractometer was proportional to the voltage applied within certain limits. Some eye muscles were severed to prevent eye movements. The cats were under nembutal anesthesia, or had been decerebrated. To prevent pupil constriction from the stimulus, partial iridectomies had been done weeks before. The results were considered analogous to the straight line relation of convergence to accommodation. Paul W. Miles.

Ogilvie, John C. **Ultraviolet radiation and vision.** A.M.A. Arch. Ophth. **50**:748-763, Dec., 1953.

The subject is reviewed under these headings: harmful effects of ultraviolet radiation, ultraviolet radiation and dark adaptation, absorption of ultraviolet rays by the eye, fluorescence and color sensations, and sensitivity of the eye to ultraviolet radiation. (4 charts, 65 references) G. S. Tyner.

Perrin, F. H. **A study in binocular flicker.** J. Opt. Soc. Amer. **44**:60-69, Jan., 1954.

When both eyes are subjected to flickering light of equal luminance and frequency, the critical fusion frequency is usually somewhat higher when the stimuli are in the same phase than when one flash is seen by one eye and alternate flashes are seen by the other. For a 2° visual target and dark surround, the difference in rate (the Sherrington effect) was proportional to the mean of the monocular critical fusion rates as target intensity was varied, and amounted to about 8 percent. Sherrington with inferior equipment had found about 3 percent difference which he considered insignificant. The effect of variation of target size with equal intensity was also studied. Some preliminary studies of stimulation of corresponding retinal peripheral areas were made. It was certain that stimulation of an area of one retina affected the sensitivity of the corresponding area of the other, but more experimentation must be done. Other experiments to determine neural interaction were proposed.

Paul W. Miles.

de Vincentiis, Mario. **The dioptric center of the eye in hypermetropia and in myopia.** Rassenga ital. d'ottal. **22**:572-576, Nov.-Dec., 1953.

With appropriate technique the author conducted experiments on the central rays of the superficial dioptrics in hypermetropic and in myopic eyes and found a plane of symmetry or its approximation. The effectual determination of the anterior and posterior angles alpha showed an increase in amplitude in hypermetropia and a decrease in myopia. The results are analyzed and discussed in the light of our present knowledge of the true construction of ocular dioptrics. (2 tables, 11 references)

Eugene M. Blake.

Wilkinson, F. R. **Some neural correlates of visual experience.** Am. J. Optometry **31**:122-126, March, 1954.

Under certain conditions a single flash of light is perceived as two. The phenomenon was studied in rabbits by means of recording electrical responses of optic nerve preparations. For certain optimum magnitudes of either duration or intensity of the flash, a double wave of impulses occurred. This was not related to the "off" effect, or to a rod and cone effect, because the flash was brief and too dim to stimulate cones. It was believed to be a retinal after-image effect.

Paul W. Miles.

Yamaji, R. **Evaluation of Yamamori's 6-6-ring as a test type.** Acta Soc. Ophth. Japan **57**:222-224, and 1512-1514, Feb. and Dec., 1953.

An evaluation of a test type introduced by Yamamori as the 6-6-ring, which is similar to Landolt's but the break of the ring is greater (60°) and the measurement is to be done in six directions, is given. The authors consider the 6-6-ring to be superior to the Landolt's.

Yukihiko Mitsui.

5
DIAGNOSIS AND THERAPY

Erpf, Stanley T. **Comparative features of plastic and/or glass in artificial-eye construction.** A.M.A. Arch. Ophth. **50**: 737-743, Dec., 1953.

The author finds plastic artificial eyes superior to glass when compared on the basis of tissue compatibility, cosmetic appearance, durability, color permanence, adaptability of form, cost and availability. A number of considerations in selection of an artificial eye are pointed out. Glass is cheaper, but the average life in use of a glass eye is 18 to 24 months, while the life of plastic eyes is much longer. Plastic eyes are more color fast, while the surface

of glass eyes may become hazy and obscure the iris colors. Plastic may be altered freely, whereas glass is much less maleable. Glass eyes may "explode" in the socket or break with handling; plastic is almost indestructible with normal use. (1 table, 6 references) G. S. Tyner.

Fowler, James G. **Transportation of normal human eyes.** A.M.A. Arch. Ophth. **50**:745-747, Dec., 1953.

The precautions for transportation and storage of human eyes are outlined. A moist chamber, non-emersion of the eye, sterility, refrigeration and proper labeling are important factors. A container for shipping is described. (2 figures)
G. S. Tyner.

Iribarren, R. **Instrument to cut lamellar corneal grafts.** Arch. oftal. Buenos Aires **28**:453-455, Oct., 1953.

The instrument described consists of two cylindrical metallic portions and one plastic part. The donor eye is placed inside the metallic portions and pressure is exercised until the cornea protrudes to the desired degree. The cornea is then flattened out by placing the plastic portion above it and is cut to the desired extension with a razor blade placed between the metallic portion and the plastic part. (2 figures) Walter Mayer.

Itō, K. **Change in the caliber of conjunctival blood vessels by eyeball compression.** Acta Soc. Ophth. Japan **57**:1529-1534, Dec., 1953.

A dilatation of the conjunctival vessels is produced by compression of the eyeball, particularly in the veins in the deeper layer. After the cessation of the compression the artery recovers its normal caliber earlier than the vein. The author considers this measurement to give some indications of the out-flow of the aqueous. (3 figures, 4 tables, 14 references)
Yukihiko Mitsui.

Kobayashi, S. **A study of experimental tuberculosis of the cornea.** Acta Soc. Ophth. Japan **57**:1441-1457, Dec., 1953.

In experimental tuberculosis in the rabbit cornea, streptomycin was ineffective clinically, but seemed to reduce the number of bacilli. Cortisone impeded the inflammation but caused an increase in bacilli. Therefore, the author recommends a combination of streptomycin with cortisone. (15 figures, 6 tables, 37 references)
Yukihiko Mitsui.

Libman, Elias. **Simple trephine for keratoplasty manufactured in Argentina and its modification for perforating keratoplasty in two planes.** Arch. oftal. Buenos Aires **28**:565-568, Dec., 1953.

Foreign corneal trephines are expensive in Argentina. The author devised one with an almost perfect cutting edge which could be manufactured in Argentina. The trephine consists of two parts, an external one and a central portion or guide, and is so constructed that a 180 degree rotation of the guide produces a cut half a millimeter in depth. When keratoplasty is done in two planes, the author has devised a modification of this trephine, which, after cutting the superficial corneal layers, cuts the subsequent ones with a smaller diameter. (2 figures)
Walter Mayer.

Pettinati, S. **The localization of orbital foreign bodies by the aid of opaque contrast media.** Rassegna ital. d'ottal. **22**:587-595, Nov.-Dec., 1953.

The author reviews the methods employed from time to time in an endeavor to improve the localization of foreign bodies in the eye and orbit. These include injection of air, oxygen, oil, and other radio-opaque substances. Experience has convinced him that the injection of water-soluble radio-opaque substances beneath Tenon's capsule, with the addition of local

anesthesia, gives the best results in those cases where a doubt exists whether the foreign body is inside the globe or outside. (3 figures, 15 references)

Eugene M. Blake.

Rocknem, Robert E. **Evaluation of wounds of the rabbit cornea treated with calsulfhydryl (hydrosulphosol).** A.M.A. Arch. Ophth. **50**:696-698, Dec., 1953.

From the author's experiments it seems evident that calsulfhydryl (hydrosulphosol) is inferior in most instances to methyl cellulose or castor oil in the treatment of controlled chemical burns of the corneas of laboratory animals. (8 references)

G. S. Tyner.

6

OCULAR MOTILITY

Arouh, J., and Zambrano, J. C. **Post-traumatic bilateral paralysis of the lateral rectus muscle.** Arch. oftal. Buenos Aires **28**:485-491, Nov., 1953.

The authors describe a patient who, two months before examination, had an auto accident which had left him unconscious for over three hours. He had diplopia when he regained consciousness. The examination revealed a marked esotropia, with complete paralysis of the lateral rectus muscles. The rest of the physical examination was negative except for a strongly positive Wassermann reaction and a very questionable fracture of both mastoid processes (found by one radiologist and denied by another). The patient was treated with penicillin and bismuth until the serologic tests became negative. He also received vitamin B in massive doses. The paralysis of the lateral rectus muscles was unmodified and even after a contemplated tenotomy of the left internal rectus, the patient would be left with a disability of at least 50 percent. The authors discuss the compensation problem. (5 figures) Walter Mayer.

7

CONJUNCTIVA, CORNEA, SCLERA

Castillo, J. L., and Filgueira, E. L. **Chloramphenicol in the treatment of trachoma.** Arch. oftal. Buenos Aires **28**: 346-352, Aug., 1953.

Fifteen patients with fairly advanced trachoma (which corresponded to the second and third stages of MacCallan's classification) were given chloramphenicol over a 30-day period. The drug was employed both orally (1.25 gr. daily in adults, and 0.75 in children) and topically (as a 5-percent ointment). Definite improvement was recorded in all cases; this seemed entirely due to the action of the chloramphenicol on the associated, secondary infections. Although representing a valuable item in the armamentarium used in such cases, chloramphenicol is less effective than sulfa drugs against the trachomatous virus itself. (9 references)

A. Urrets-Zavalía, Jr.

Friede, Reinhard. **Keratoplasty and scleroplasty in the treatment of ocular tumors.** Ophthalmologica **126**:295-307, Nov., 1953.

In a number of situations occurring in the treatment of epibulbar and intraocular tumors keratoplasty or scleroplasty may be of greater value than heretofore realized. After the surgical removal of a typical limbic dermoid the author filled the resultant corneal defect with an accurately fitted lamellar corneal graft. An epithelioma of the cornea not involving the limbus or sclera was removed radically by excising tumor and host tissue down to the level of Descemet's and replacing it with a full thickness corneal graft. A basal cell carcinoma of the bulbar conjunctiva close to the limbus was removed radically by excising it with the surrounding and underlying sclera and replacing it with a full thickness corneal graft. The author

envisions the use of similar procedures for the treatment of malignant, but circumscribed, tumors of the peripheral iris or ciliary body. (8 figures)

Peter C. Kronfeld.

Kruemmel, H. **Sarcoid of the conjunctiva.** Ophthalmologica **126**:193-208, Oct., 1953.

Among the patients of a lupus sanitarium in West Germany the author found seven cases of benign granuloma of the conjunctiva which on histologic examination proved to consist of well defined nodules made up of epithelioids surrounded by lymphocytes. A definite, argentophilic reticulum could be recognized in these nodes. Giant cells were fairly common; they were the only elements undergoing colliquation necrosis. In general, the nodes were gradually absorbed, leaving only slight hyaline and fibrous residues. The author considers these lesions as typical manifestations of Boeck's disease in the conjunctiva. They are probably very common, but often overlooked since they cause no subjective symptoms. In none of the author's cases would any treatment have been necessary. Discovery and biopsy of such benign granulomas may be helpful in diagnosing the systemic disease. (20 figures, 15 references) Peter C. Kronfeld.

Malbrán, J. L., Paunessa, J. M., and Vidal, F. **Hereditary crystalline degeneration of the cornea.** Ophthalmologica **126**: 369-378, Dec., 1953.

One thoroughly studied case of this typical hereditary corneal degeneration is reported (cfr. Forni, Am. J. Ophth. 35: 898, 1952; Sherman, Am. J. Ophth. 25: 1019, 1942). A visually successful lamellar keratoplasty yielded material for histologic study. (9 figures, 3 references)

Peter C. Kronfeld.

Pavišić, Zvonimir. **Surgical treatment of trachomatous symblepharon.** Ophthalmologica **126**:240-244, Oct., 1953.

According to the author's experiences in Jugoslavia, trachomatous symblepharon begins in the inner canthus and spreads from there to the lower fornix. In three such cases the author obtained a good result by using all existing remnants of conjunctiva to cover the lower lid and a buccal mucous membrane flap to cover the globe. Multiple anchorage of the latter to the underlying structures, particularly the recti muscles, seemed important. The dissection was started at the limbus and in the horizontal meridian of the bulbar conjunctiva. (5 figures, 10 references) Peter C. Kronfeld.

Pirodda, Andrea. **Hypopyon corneal ulcer due to bacillus pyocaneous.** Rassegna ital. d'ottal. **22**:566-571, Nov.-Dec., 1953.

A 13-year-old boy presented a nontraumatic, deep central ulceration of the right eye. No micro-organisms were isolated and apparent healing occurred in 12 days. Treatment consisted of the administration of penicillin and sulfa drugs. A few days after apparent recovery the ulcer broke down and increased in severity. The introduction of material from the ulcer produced a very severe ulceration in the rabbit eye, which had been first abraided. Cultures from the rabbit eye showed Pseudomonas aeruginosa. Treatment with terramycin led to prompt recovery. (1 figure, 16 references)

Eugene M. Blake.

Salleras, Alejandro. **Indications and contraindications of keratoplasties.** Arch. oftal. Buenos Aires **28**:498-504, Nov., 1953.

During the past two years, the author has done 172 keratoplasties. The main indications for keratoplasty are optical defects, the need to reestablish normal

corneal structure, preparation for a second transplant, and cosmetic. As a general rule a keratoplasty should not be performed if the visual acuity is better than 1/10. All ocular infections, severe general or mental diseases, and defective light projection are contraindications for this procedure.

In order for a perforating keratoplasty to be successful, it is necessary that half of the donor cornea be in contact with normal cornea, and it should not be greater than eight millimeters in diameter. It is useful in keratoconus, deep, circumscribed opacities of traumatic, syphilitic, or tuberculous origin, disciform keratitis and adherent leucoma, descematocele, and in macular corneal dystrophies which are recessive. A total penetrating keratoplasty would be indicated in cases of total leucomata which are very vascularized and porcelain-like. If there are numerous anterior synechiae, a total excision of the iris should be done to prevent secondary glaucoma.

The lamellar graft is indicated because it is a less daring operation, and the postoperative course is much shorter. However, such types of graft become infected or necrotic more easily. This type is highly recommended when perforating keratoplasty is dangerous, as in one-eyed subjects, nystagmus, aphakia, children, very old patients, and psychopaths. This type is also indicated in the dominant familial corneal dystrophies in which the deeper corneal layers are normal, in the very superficial or very vascularized leucomata, in alkali burns of the cornea, as a preparatory operation for a perforating keratoplasty, in certain types of keratitis, such as herpetic serpiginous ulcer and interstitial keratitis, which respond poorly to treatment, for cosmetic reasons in amblyopic eyes, in moderate degrees of keratoconus, and in descematocele.

Walter Mayer.

Salleras, Alejandro. **Preparation of the eye and of the patient before undergoing a keratoplasty.** Arch. oftal. Buenos Aires **28**:535-539, Dec., 1953.

The author emphasizes the necessity of doing only a keratoplasty at the time of operation; all preliminary surgery should have been completed at a previous stage. All infections of lids and lacrimal system should be cleared up previously and the eye should be quiet for at least six months after uveitis before a keratoplasty is attempted. One of the greatest problems is the ocular hypertension, which in cases of deformed corneas is sometimes difficult to diagnose. In these cases, the author uses Wolfe's scleral tonometer. A catract is no contraindication for a keratoplasty, but the transplant should be done before the lens extraction. A severe corneal vascularization should be treated with beta radiation before the keratoplasty is done. The author uses a combination of an antihistamine, ergotamine, luminal, and ampliatil (a hypnotic drug) to obtain a "pharmacological lobotomy," disconnecting the patient completely from his surroundings.

Walter Mayer.

Salleras, Alejandro. **Preservation of cornea for keratoplasties.** Arch. oftal. Buenos Aires **28**:509-511, Nov., 1953.

The author reviews the experimental work which has been done in substituting for the cornea some type of plastic material, and concludes that all of such grafts are extruded sooner or later. He recommends that eyes should be enucleated from donors twelve hours after death in winter, and no more than six hours after death in summer. Corneas from older people are better than those from a fetus, because they have a better curvature and thickness. The enucleated eye should be placed in a vial with saline solution and should be irrigated with penicillin solution. It should then be placed in the

refrigerator at 2° C. If the cornea is free of nubeculae and macroscopically visible folds in Descemet's membrane, it may be used for a penetrating keratoplasty. If folds are present, it may be used for a lamellar graft. The author emphasizes the great advantage of using the eyes as early after enucleation as possible, even though they may be preserved in the refrigerator for ten days. Walter Mayer.

Salleras, Alejandro. **Technique of perforating keratoplasty.** Arch. oftal. Buenos Aires **28**:569-574, Dec., 1953.

The author describes his personal technique. Anesthesia is produced by topical instillation of cocaine, and akinesia is produced with tubocurarine. A retrobulbar injection is used only rarely. If the donor graft is smaller than eight millimeters, it is cut entirely with the trephine; if it is greater, Castroviejo scissors are used to complete the section. One suture is then placed in the graft, and the same trephine is used to cut the recipient cornea. Care should be taken to center the trephine precisely, because if it is placed at any other point, a severe astigmatism may result.The author prefers corneo-corneal sutures, and the points of entry and exit of the sutures should not be more than 0.3 millimeters away from the section, in order to give perfect coaptation. At the end of the procedure, he fills the anterior chamber with saline solution and places additional sutures if the wound is not watertight. (2 figures)

Walter Mayer.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Bignell, John L. **A malignant melanoma of the choroid oculi.** Australian & N.Z.J. Surg. **23**:236-239, Feb., 1954.

A case of malignant melanoma showing three distinct cell types and combining the raised form with the flat infiltrating type is reported. Ronald Lowe.

Busacca, Archimède. **A new observation in the anterior vitreous in cases of uveitis.** Ophthalmologica **126**:354-360, Dec., 1953.

The new observation concerns the shape of the retrolental space in some cases of uveitis. In the normal eye this space shows, on slitlamp examination, a triangular cross section with its apex back and down in the vitreous. Its posterior boundary, the membrana plicata of Vogt, is adherent to the periphery of the posterior lens capsule and separates from the latter in the more axial portions of the eye. That relationship should give the retrolental space an approximately semispherical shape, were it not for some gravitational forces pulling back and down on the plicate membrane and the lamellae behind it. In some cases of uveitis the relative specific gravities of the structures in the anterior vitreous are altered, causing the plicate membrane and the retrolental space to assume a new shape. (3 figures) Peter C. Kronfeld.

Sená, Jose A. **Sympathetic uveo-papillitis.** Arch. oftal. Buenos Aires **28**:337-345, Aug., 1953.

Serous uveitis represents a much milder form of sympathetic disease than the classically known, extremely severe plastic iridocyclitis. Uveo-papillitis, a condition observed as an exceptional complication of anterior uveitis, is responsible for a sudden, marked decrease in vision which depends upon the development of a central scotoma (cf. Jayle, G. E., Ourgaud, A. G., and Brémond, J.: Bull. Soc. Franc. Ophtal., 61:227, 1948), and may be of a sympathetic origin.

The case of a 30-year-old man, with a penetrating wound of one eye and retention of an intraocular foreign body, is

described. Although a steel particle was removed after the accident, vision could not be preserved, and enucleation had to be performed after a delay of one month. Pathologic examination revealed the typical picture of sympathetic endophthalmitis. Three weeks later a pronounced reduction in the visual acuity of the remaining eye was noted; aside from a slight cyclitis, a severe congestion of the optic nerve head and a pale retinal edema of the posterior pole were detected. A nearly absolute central scotoma accounted for the visual loss. Systemic administration of large doses of cortisone over a five-weeks period resulted in complete and permanent recovery. (4 figures, 8 references) A. Urrets-Zavalía, Jr.

Szekler, Robert. **Uveal sarcoma associated with neurofibromatosis.** Ophthalmologica **126**:248-251, Oct., 1953.

The subject of this paper is a 20-year-old woman with neurofibromatosis in the form of multiple small skin tumors and café-au-lait spots. Her mother and one aunt had the same disease. The patient came to the eye clinic because of a tumor of the anterior uvea which filled half of the anterior chamber of one eye. Enucleation was not performed until a year later and revealed a malignant, partly necrotic spindle-cell tumor, which was diagnosed sarcoma. Eighteen months later the patient was readmitted with marked enlargement of the liver and cachexia. Autopsy was not performed. (1 figure, 6 references) Peter C. Kronfeld.

9

GLAUCOMA AND OCULAR TENSION

Cascio, Giuseppe. **Biological aspects of the anti-glaucomatous activity of fisostina.** Rassegna ital. d'ottal. **22**:577-582, Nov.-Dec., 1953.

Fisostina is furfuriltrimethyl-para-toluensolfonate, a new colinergic preparation. The drug produces a lowering of blood pressure by general dilatation of blood vessels. Its action upon the eye is to induce miosis and contraction of the ciliary muscle, thus opening the angle of the anterior chamber. Fluorescein appears in the angle sooner than in untreated eyes. (1 figure, 12 references)

Eugene M. Blake.

Haas, Joseph S. **Glaucoma.** A.M.A. Arch. Ophth. **50**:764-778, Dec., 1953.

The pertinent literature for 1952-53 is reviewed under four main headings: primary glaucomas, diagnosis, medical and surgical treatment. (93 references)

G. S. Tyner.

Ljustina-Ivančić, Vevenka. **Tetraethylammonium in the treatment of glaucoma.** Ophthalmologica **126**:378-387, Dec., 1953.

The effect upon the ocular tension of the ganglionic blocking agent tetraethylammonium bromide was studied in 15 cases of glaucoma (cfr. Drucker, Sadove and Unna, Am. J. Ophth. 33:1504, 1950). The drug was administered intramuscularly twice daily for 12 to 14 days in doses of 20 to 30 mg./Kg. of body weight. Slight lowering of the ocular tension could be observed, particularly in cases with coexistent cardiovascular hypertension. Tetraethylammonium bromide is not a specific antiglaucomatous agent, but its transient depressing or pressure-lowering effect may be of value in preparing a hypertensive individual for surgery. (2 figures, 2 tables, 17 references)

Peter C. Kronfeld.

Matteucci, Pellegrino. **Ophthalmotonic arrhythmia in chronic glaucoma.** Rassegna ital. d'ottal. **22**:545-555, Nov.-Dec., 1953.

The author points out that there is a regular oscillation of ocular tone in normal eyes; the tension is elevated in the

morning and the lowest in the evening. In chronic glaucoma there are many modifications of this pattern. For many years at the Torino clinic, a daily tension curve has been taken on all glaucoma patients and the author feels that he can differentiate the changes due to normal arrhythmia from those of glaucoma. This makes the administration of miotics more accurate. Normal ophthalmotonus varies about 10 mm. during the day. In glaucoma, the base curve is elevated. Most glaucoma patients have inadequate concentration of miotics and the use of methylcellulose is urged. (9 figures, 24 references)

Eugene M. Blake.

Radnót, M., and Orbán, T. **Experimentally produced rise of ocular tension in the rabbit.** Ophthalmologica **126**:245-247, Oct., 1953.

Continuing their studies on the relationship between function of the gonads and ocular tension, the authors ligated one deferent duct in nine rabbits. Two of the seven surviving rabbits showed unilateral rises in ocular tension. In the remaining five animals no changes in ocular tension could be observed. (1 figure, 9 references)

Peter C. Kronfeld.

10

CRYSTALLINE LENS

Corrado, Antonio. **Operation for secondary cataract.** Rassegna ital. d'ottal. **22**:529-544, Nov.-Dec., 1953.

The various procedures for the treatment of secondary cataract are reviewed and the many unsatisfactory results of these operations after an extracapsular extraction are described. Such matters as the frequency of secondary cataract, the type of incision preferred and the complications after the various procedures are described as reported by many surgeons. The writer prefers to use the double-edge knife of Guglianetti since no traction is made on the ciliary body and no complications are encountered. Introduction of the knife at the limbus preserves the integrity of the irido-corneal angle. (83 references)

Eugene M. Blake.

Konstas, Konstantin A. **Cataracta centralis.** Ophthalmologica **126**:231-239, Oct., 1953.

Congenital central cataract occurred in three kindreds of a small, presumably Greek, family. Despite some variations in the size and shape of the opaque area, central cataract is a typical entity; it is dominantly inherited and in most cases requires no treatment. (3 figures, 13 references)

Peter C. Kronfeld.

11

RETINA AND VITREOUS

Shimizu, T. **Basal metabolism of patients with pigmentary degeneration of the retina.** Acta Soc. Ophth. Japan **57**: 1491-1494, Dec., 1953.

In 10 of the 38 patients examined, there was a slight increase in the basal metabolism. A decrease was found in none. (3 tables, 24 references)

Yukihiko Mitsui.

13

NEURO-OPHTHALMOLOGY

Chamlin, Max. **Visual field changes in optic neuritis.** A.M.A. Arch. Ophth. **50**: 699-713, Dec., 1953.

100 cases of optic neuritis or retrobulbar neuritis are reported with regard to visual field changes. There were some unusual findings. 21 to 37 percent of patients had normal or nearly normal central visual acuity; 24 percent showed marked peripheral rather than central field defects. In cases with peripheral field defects, the lower nasal field was most frequently involved. Only 52 percent showed a cecocentral scotoma. The author concludes

that maintenance of good central acuity cannot be regarded as a major criterion for differentiating optic neuritis from papilledema. (8 figures, 9 references)

G. S. Tyner.

Gartner, Samuel. **Optic neuropathy in multiple sclerosis.** A.M.A. Arch. Ophth. **50**:718-726, Dec., 1953.

The autopsy findings of sections of the optic nerve in cases of optic neuritis due to multiple sclerosis are reported in 14 eyes of 10 patients. The essential finding was optic atrophy with extension to the nerve fiber layer and the ganglion cells, particularly in the macular area. The author believes that the commonest type of optic neuritis is secondary to chorioretinopathy from any cause. He doubts the validity of the term neuritis as applied to involvement of the optic nerve in multiple sclerosis, since it is essentially a degenerative process. (6 figures, 13 references)

G. S. Tyner.

Kaeser, Ernst H. **The arteriovenous aneurysm in the cavernous sinus.** Ophthalmologica **126**:257-282, Nov., 1953.

Practically a treatise on arteriovenous aneurysms in the cavernous sinus, this report from the neurosurgical unit of the University of Zurich will be of great interest to the ophthalmologist. Thirteen cases are described in detail. Ligation of the common, external and internal carotid artery in the neck was performed in eight cases, resulting in two cures and four improvements. One patient died shortly after the ligation from sequelae of the original accident but not as the result of the ligation. The risk entailed in the ligation is small, principally because the development of the aneurysm has greatly reduced the significance of the ipsilateral carotid as a provider for the brain. If the cervical ligation is of no effect, the intracranial ligation of the internal carotid offers a fair chance of a cure. In case of failure of both arterial ligations the orbital veins may be ligated. Healing of the aneurysm occurs through a process of thrombosis. (5 figures, 25 references)

Peter C. Kronfeld.

Ulett, George A. **Flicker sickness.** A.M.A. Arch. Ophth. **50**:685-687, Dec., 1953.

Intermittently flashing light is used to produce abnormal rhythms in the electroencephalogram in the diagnosis of epilepsy and to trigger seizures in the convulsive treatment of psychotic patients. In both patient and examiner the stimulus can produce dizziness, nausea and psychic phenomena. (5 references)

G. S. Tyner.

Venco, L., and Morone, G. **Pupillary manifestations of contusion of the eyeball.** Ophthalmologica **126**:282-289, Nov., 1953.

The pupillary reactions of 15 cases of contusio bulbi were studied pupillographically (continuous photographic recordings after Loewenstein) and under the influence of drugs. Five types of neuromuscular disturbance could be recognized. Paralysis of the parasympathetic innervation was very prevalent. The sympathetic was in a state of irritation in a few cases. (6 figures)

Peter C. Kronfeld.

14

EYEBALL, ORBIT, SINUSES

Glees, M. **Bilateral microphthalmus in a case of prenatal toxoplasmosis.** Ophthalmologica **126**:361-368, Dec., 1953.

A male baby, born one month prematurely was admitted to the pediatric clinic of the University of Cologne in poor general condition. The outstanding clinical findings were hydrocephalus of excessive degree and bilateral microphthalmus. Death from pneumonia occurred about four weeks later. The au-

topsy revealed typical toxoplasmic, granulomatous and necrotizing meningo-encephalitis. Innumerable toxoplasmic pseudocysts could be identified in the remnants of the frontal lobe. Both cerebral hemispheres had been transformed into large, thin-walled cysts.

Both eyeballs and their adnexa were in the state of microphthalmus. Choroid and retina showed little active inflammation, but gross derangement and distortion of cell layers with multiple cyst formations. The visual epithelium was practically absent and an overgrowth of glia had taken its place. Only the sheaths of the optic nerve showed marked active inflammation. Although no toxoplasmic parasites could be found in the eyes, there can be no doubt about the originally toxoplasmic nature of the ocular lesions. The case is presented as an illustration of the polymorphism of ocular toxoplasmosis. (11 figures, 4 references)

Peter C. Kronfeld.

Henderson, John W. **Reconstruction of the orbit with polyvinyl sponge.** A.M.A. Arch. Ophth. **50**:714-717, Dec., 1953.

With the use of the polyvinyl sponge, no anchoring sutures are necessary. The operative procedure is further simplified by easy shaping of the sponge to the existing defect. In a two-year follow up no untoward inflammatory reaction has been noted. It is believed the sponge acts as a framework for the growth of normal tissue. (3 figures, 4 references)

G. S. Tyner.

15

EYELIDS, LACRIMAL APPARATUS

Erausquin, H., and Ferrer, A. **Traumatic foreign body in the lacrimal sac.** Arch. oftal. Buenos Aires **28**:446-452, Oct., 1953.

The authors describe the case of a patient who had a piece of metal in the inner portion of his orbit. An attempt to remove it failed and lacrimation continued. The lacrimal passages were patent, but on applying the electromagnet over the lacrimal area, the patient had severe pain and lacrimation was greatly increased. An incission was made as for a dacryocystectomy and the foreign body removed with forceps. The authors review briefly the literature available on foreign bodies inside the lacrimal sac. Most of them are introduced accidentally through the canaliculus or the nose. There is no previous record of a traumatic foreign body directly in the sac. (4 figures)

Walter Mayer.

Malbran, Jorge L. **Lacrimal intubation, a new technique.** Arch. oftal. Buenos Aires **28**:512-519, Nov., 1953.

The author believes that dacryocystorhinostomy is too extensive an operation for the relief that is expected and also it is uncertain in its results, despite numerous cures obtained with it. He reviews very thoroughly the attempts which have been made to intubate the lacrimal passages with different materials and in different ways. He then describes his own procedure, he anesthetizes the lacrimal canaliculi, the sac and lacrimonasal duct very carefully with pontocaine and xilocaine. He then introduces a Weber canaliculus knife into the lower canaliculus and sac, and splits the entire canaliculus; he then elevates the handle of the knife and cuts the nasolacrimal duct and repeats the same procedure in the upper canaliculus and unites both incisions by severing the mucous union at the inner canthus. He passes a Bowman probe covered by a polyethylene tube through the canaliculus into the nose and removes the probe. The tube is left in place. The author has had good success in six cases. In two others the tube was extruded, but was easily replaced. (26 references)

Walter Mayer.

Pereira, Roberto F. **The use of electrocoagulation in dacryocystorrhinostomy.** Arch. oftal. Buenos Aires **28**:575-577, Dec., 1953.

Since hemorrhage may be a severe complication during and after a dacryocystorrhinostomy, the author, following the procedures of Barraquer, has used the electric bisturi for skin and nasal mucosa incisions. In one of his patients the cutaneous incision reopened, and two others became infected. He now uses the electric bisturi only for the incision of the nasal mucosa, and has thereby eliminated hemorrhage during and after the procedure. To avoid perforation of the nasal septum, he uses a spatula introduced into the corresponding nostril to give counterpressure to the electric bisturi. (4 references) Walter Mayer.

Tillisch, A. E. **Comments on the use of the ptosis crutch.** Am. J. Optometry **31**: 137-139, March, 1954.

The case of a patient with complete bilateral ptosis who had worn the ptosis crutch for 24 years is reported. She was greatly relieved after "medical resources had been exhausted without help."

Paul W. Miles.

17

INJURIES

Zambrano, J. C. **Ocular lesions produced by indelible pencils.** Arch. oftal. Buenos Aires **28**:475-477, Oct., 1953.

The author reports the case of a patient who after getting some particles of an indelible pencil into his eyes, irrigated them with raw milk and obtained white eyes in a few hours. Experimentally the author repeated this same treatment in rabbits, with good results. In three other patients whom the author has seen since, this treatment has been successful and the treatment of such lesions, which used to be of long duration, is considerably shortened.

Walter Mayer.

18

SYSTEMIC DISEASE AND PARASITES

Arouh, J., and Silberstein, M. **A case of pemphigus vulgaris.** Arch. oftal. Buenos Aires **28**:408-412, Sept., 1953.

The author describes a patient with pemphigus, which was first diagnosed because of the lesions in the eye. After a stage of acute conjunctivitis with severe chemosis, some vesicles developed over the bulbar conjunctiva. The author reviews briefly the eye signs in this disease and emphasizes that the most important ocular feature is not the formation of vesicles, but the invasion of the submucous tissue by new connective tissue, which brings about the subsequent contracture. (1 figure, 26 references)

Walter Mayer.

Arouh, J., Zambrano, J. C., and Lis, M. **Ocular symptoms of botulism. Report of two cases.** Arch. oftal. Buenos Aires **28**: 317-325, July, 1953.

An extremely severe food poisoning caused by the toxin of Clostridium botulinum, botulism, is due to the consumption of improperly canned or preserved aliments and consist mainly of vomiting, abdominal pain, constipation or, less commonly, diarrhea, nervous symptoms of central origin, disturbances of secretions and weakness of the voluntary muscles, among which those supplied by the third, fourth, sixth, ninth and tenth cranial nerves are most frequently affected. Mydriasis and paralysis of accommodation are early, cardinal symptoms. A fatal course is observed in about one half of all cases, and recovery is slow in those who recover.

Two cases are reported. In one of them, death occurred on the tenth day after the ingestion of the contaminated food, a

homemade salad dressing, in spite of the administration of large doses of polivalent botulinus antitoxin. In the other, in which recovery took place, accommodation was still poor one year after the accident.

A. Urrets-Zavalia, Jr.

Cambiaso, R. H. **Ocular ocronosis with alkaptonuria and osteoarthritis.** Arch. oftal. Buenos Aires **28**:456-474, Oct., 1953.

The author presents a case of alkaptonuric ocronosis with its typical triad: pigmentation of cornea and sclera, alkaptonuria and osteoarthritis deformans. This is the first paper about this subject in the ophthalmic literature of Argentina and the seventh publication about alkaptonuria in Argentina. After emphasizing the symptoms present in the locomotor system and the typical changes which occur in the alkaptonuric urine, the author describes in detail the changes occurring in conjunctiva, cornea and sclera and reviews the ocular findings reported by others. (6 figures, 2 tables, 131 references)

Walter Mayer.

Guerrero, Rafael A. **First case of onchocercosis diagnosed clinically in Caracas.** Arch. oftal. Buenos Aires **28**:418-426, Sept., 1953.

In a patient who complained of photophobia and burning of both eyes, the slitlamp examination revealed the existence of freely floating parasites in the aqueous of both eyes. A clinical diagnosis of onchocercosis was made, which was confirmed by the positive finding of these parasites in biopsies of skin nodules. The author was able to obtain a photograph of one of the parasites in the anterior chamber, a difficult task because of their negative phototropism, by replacing the right ocular of a Haag Streit slitlamp with the microphotographic attachment of a Leica. The patient was given Hetrazan for fifteen days, after which no more parasites were seen in the aqueous. Eight months after the first treatment, more parasites were discovered in the aqueous, but these disappeared after three more days of the same treatment. (3 figures, 23 references)

Walter Mayer.

Howells, Leonard H. **Ocular complications of diabetes mellitus.** Brit. J. Ophth. **37**:716-724, Dec., 1953.

Diabetes is hereditary and is transmitted as a Mendelian recessive. Since insulin, there has been an increase in the fertility of diabetics, a reduction in the incidence of maternal mortality, and an improvement in the fetal survival rate. Diabetics may live almost as long as nondiabetics. Factors influencing the development of diabetes are hereditary transmission, infections and sepsis, obesity, and disorder of endocrine glands. The disease is usually mild when it appears for the first time between the ages of 40 and 65. Although the disease in a severe form may affect all ages, it is especially apt to occur in those under the age of 20 or over 65 years.

Ocular complications are frequent and distressing and are becoming more common because of the increasing longevity of diabetics. Retinopathy occurs even in mild and well-controlled diabetes. Diabetic retinopathy is independent of and distinguishable from the effects of arteriosclerosis and hypertension. In the later stages retinal changes characterized by hypertension may be superimposed on those due to diabetes, and in advanced cases it may be impossible correctly to apportion the blame. Retinitis proliferans is known to occur as a late complication of diabetic retinopathy in long-standing cases, the retinal changes being accompanied by severe damage to the kidneys and hypertension. Kimmelstein-Wilson disease is also one which occurs in long-standing diabetes, and is characterized by

renal and retinal lesions resulting in early death from renal or cardiac failure, or in blindness. Its essential lesion is an intercapillary glomerosclerosis.

The fundus picture in diabetes is progressive and the prognosis is bad. Temporary changes in accommodation causing either myopia or hypermetropia may result from changing refraction due to varying sugar content, particularly in patients receiving insulin. Retrobulbar neuritis and diplopia occur occasionally, and, more rarely, lipemia retinalis, optic tract lesions, optic atrophy, and paralysis of the ocular muscles may be encountered.

Orwyn H. Ellis.

Miratynska, E., and Krawczyk, Z. **Three cases of severe ocular complications in arterial hypertension.** Klinika Oczna **23**:189-193, 1953.

The authors describe three cases of severe ocular lesions in the course of arterial hypertension. The patients had hypertensive retinopathy and retinal detachment. (2 figures, 11 references)

Sylvan Brandon.

Schirmer, R. **Temporal arteritis with ocular involvement.** Klin. Monatsbl. f. Augenh. **124**:58-63, 1954.

In a 77-year-old man with bilateral occlusion of the central retinal artery, the excised temporal artery revealed the typical picture with necrosis and a granulation tissue containing giant cells. (4 figures, 1 table, 16 references)

Frederick C. Blodi.

Scott, G. I. **Ocular complications of diabetes mellitus.** Brit. J. Ophth. **37**:705-715, Dec., 1953.

The retinal changes which may occur in diabetic patients are by far the most important ocular complication of the disease. The incidence of retinopathy increases with the duration of the disease and is in no way related to the severity of the diabetes. At the beginning, the process is largely in the walls of the veins and produces multiple micro-aneurysms, and perhaps a few hemorrhages. Occasionally changes occur in the larger veins, which may be distended and looped or coiled. Escape of blood into the deeper layers of the retina follows with or without the formation of exudates. As the disturbance progresses the process gradually changes to dot and blot hemorrhages, with more confluent exudates.

In a minority of patients in whom further deterioration occurs, the disease follows one of two very different courses. A certain number of cases show an exacerbation. In other cases a sudden hemorrhage into the vitreous may occur, which will inevitably be followed by the development of retinitis proliferans. In retinitis proliferans, nearly 90 percent of the patients had had diabetes for more than five years. The appearance of a few micro-aneurysms or hemorrhages in the fundus of a diabetic does not necessarily mean that he will suffer early impairment of vision, since serious macular destruction may not occur for many years. Marked congestion of the veins and the occurrence of superficial blots of hemorrhage offer a much worse prognosis than scattered deep hemorrhages and exudates. There is no correlation between the occurrence of vascular or retinal changes and the control of the diabetic state. Truly strict control of the diabetic state might lessen the incidence of degnerative changes. On the other hand, there is no doubt that in certain cases the diaster of hemorrhage into the vitreous occurs as a vascular accident in patients with only a few retinal hemorrhages, and perfectly controlled diabetes.

Capillary fragility is increased in a large portion of patients with diabetic retinopathy. Sudden changes in refraction

occur which are doubtlessly due to a change, probably hydration, in the lens. True diabetic cataract, which is bilateral and often develops quickly, occurs in young patients with severe diabetes and is relatively rare. Senile cataract is no more common in diabetics than in others, but seems to mature more quickly in the diabetic. The most serious post-operative complication of extraction is iritis or iridocyclitis which may be severe and intractable. Orwyn H. Ellis.

Torres-Estrada, Antonio. **Ocular invasion by microfilariae in cases of onchocerciasis.** Arch. oftal. Buenos Aires **28**: 353-365, Aug., 1953.

The presence of young filarial worms in the anterior chamber and the cornea of the living eye, as well as the pathogenesis and the course of the ensuing lesions, have been demonstrated chiefly by Mexican ophthalmologists. Four stages may be recognized as the ocular involvement progresses in cases of onchocerciasis. 1. At the stage of invasion—which occurs via the lymphatic system—, microfilariae are seen in the anterior chamber and in the anterior part of the vitreous; the parasites adopt a vertical disposition and appear like fine, iridescent, slowly moving filaments. No reactional phenomena occur at this time. 2. As the filariae penetrate the posterior layers of the corneal parenchyma and die, they are surrounded by a slight infiltration and some degree of punctate keratitis becomes manifest; if adequate treatment is then started, the lesions may disappear completely. 3. If the condition is neglected, the latter become widespread and tend to be confluent; the parasites can no longer be seen, and a severe, nonreversible reduction in vision takes place. 4. In more advanced cases, uveal complications, secondary glaucoma and blindness supervene.

In addition to slitlamp microscopy, ophthalmoscopy may be of great help in the detection of the microfilariae, provided a special technique is followed.

A. Urrets-Zavalia, Jr.

Velzeboer, C. M. J. **Ocular manifestations in Loffler's syndrome.** Brit. J. Ophth. **37**:731-740, Dec., 1953.

The literature is reviewed in detail. Loffler's pneumonia is a harmless disease; the infiltration in the lung is very fugitive. In the author's patient the abnormalities of the right eye, though extremely variable in extent, did not disappear completely. It can be supposed that the very dense infiltration of the retina, mainly with eosinophilic cells, transudation (edema), and focal necrosis, must be held responsible for the irreversible lesion of the nerve-fiber layer, and caused the defects in the visual fields. The infiltration seemed to be near to the veins rather than the arteries. The visual field defects recall Jensen's juxtacapillary chorioretinitis, but in this patient the inflammation and the scars were restricted to the retina and differed from the typical chorioretinal scars in Jensen's disease, and the pigment-epithelium was not disturbed. Moreover, the visual field defect of the left eye, with a normal fundus picture, could only be attributed to a local affection of the left optic nerve.

The blood eosinophilia persisted for more than a year after the healing of the process in the retina and lung; and therefor cannot be due to a resorption eosinophilia, as suggested by Loffler. It must be identical with the blood eosinophilia in allergic conditions, which is supposed to be an allergic response of the bone marrow. Orwyn H. Ellis.

19

CONGENITAL DEFORMITIES, HEREDITY

Charlin, Carlos. **van der Hoeve syn-**

drome. Arch. chil. de oftal. **10**:45-54, Jan.-June, 1953.

The author reviews briefly the chief symptoms of this syndrome and relates the clinical history and findings on two patients who presented the typical syndrome. He concludes that it is a congenital and hereditary disease without known treatment. (8 figures, 5 references)

Walter Mayer.

François, J., and Deweer, J. P. **Fundus changes characteristic of the female-carrier state of sex-linked ocular albinism in the male.** Ophthalmologica **126**:209-221, Oct., 1953.

Fourteen cases of sex-linked, ocular albinism in the male occurred in a Belgian family comprising five generations and 187 kindreds. The most interesting feature was the fact that the carrier-state could be recognized in female members of the family by a very striking, irregular pigment distribution in the periphery of the eyeground (cfr. Falls, Am. J. Ophth. 34:41-50, part II, May, 1951. (5 figures, 9 references) Peter C. Kronfeld.

Tosi, Bruno. **Persistent pupillary membrane.** Arch. oftal. Buenos Aires **28**:540-545, Dec., 1953.

Five siblings who had varying degrees of a persistent pupillary membrane are described. The parents and another brother did not show any signs of such an anomaly. (7 figures, 9 references)

Walter Mayer.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Charamis, J. **Present status of trachoma in Greece.** Rev. intern. du trachome **30**: 475-479, 1953.

According to the author, the trachoma index for Greece 20 years ago was 4 percent, but at present, though varying widely from region to region, is only 1 percent for the country as a whole, with more women affected than men. Fresh infections are becoming rare, thanks to an anti-trachoma campaign started in 1925, and the complications are less severe. The reduction in the incidence of trachoma is not paralleled by a similar reduction in the incidence of seasonal conjunctivitis. (10 references) Phillips Thygeson.

Etzine, S. **Some ecological techniques in trachoma.** Rev. intern. du trachome **30**:527-530, 1953.

The science of ecology is concerned with the relation of different living organisms to each other and to their habitat, and ecological techniques are used primarily by botanists to study changes in plant life. Etzine suggests applying these techniques to the study of trachoma in South Africa. As in the botanical survey, a preliminary reconnaissance could be made and areas for detailed study chosen. The total population in the selected "quadrat" would then be examined and all ocular diseases recorded. The quadrat would be reexamined at intervals of a year or two to note the nature of any changes which might have occurred and to determine their cause. The climate of the area, the water supply, the insect population, and the economic and nutritional status of the population would be noted. Trachoma could be cleared in a limited zone as a pilot scheme for working out the best methods applicable to the country as a whole and for determining costs. Secondly, the manner of reinfection could be studied. The author elaborates other techniques which might be applied to trachoma and concludes that the application of these ecological principles should yield useful information.

Phillips Thygeson.

Foster, John. **The legend and shrine of Saint Triduana.** Brit. J. Ophth. **37**:763-765, Dec., 1953.

When pestered by a suitor, Saint Triduana is believed to have performed an auto-evulsion of her eyes and sent them to him. Foster tells legend and history and describes the church, shrine, and statue. (1 figure) Orwyn H. Ellis.

Hadi Rais. **The campaign against purulent ophthalmia, with particular reference to the use of a mobile therapeutic team.** Rev. intern. du trachome **30**:518-526, 1953.

The problem of the prevention of blindness in North Africa and the Near East is primarily one of controlling the purulent ophthalmias, particularly gonococcal ophthalmia. The present campaign in Tunisia was started in 1951 for the systematic mass treatment of the seasonal ophthalmias throughout the territory of the Regency. The campaign utilizes various educational means, including radio programs, posters, and pamphlets for the general population, refresher courses for the general physicians and nurses, and special courses for nursing aids, midwives, social workers, and police. In the campaigns of 1951 and 1952, 1 percent aureomycin ointment was found to be most efficacious against Koch-Weeks conjunctivitis. Bacteriologic examinations for the recognition of gonococcal ophthalmia were made in all cases showing corneal lesions. A mobile unit was formed primarily for the purpose of detecting and extinguishing epidemics of this disease. The findings in several epidemics are recorded. It is concluded that the campaign has been successful in saving many individuals, particularly children, from blindness.

Phillips Thygeson.

Siebeck, R. **Map of trachoma in Europe and the Near East.** Rev. intern. du trachome **30**:537-541, 1953.

The first volume of the World Atlas of Infectious Diseases, edited by Professor E. Rodenwaldt of Heidelberg, appeared in 1952. Trachoma is represented in this atlas by a map accompanied by an explanatory text. The statistical documentation of the map is based on an analysis of material from the ophthalmological literature of the past 30 years. The map shows the principal endemic areas to be in the Middle East and bordering the Mediterranean. Phillips Thygeson.

Ophthalmic Miniature

Should one eye only be affected, the operation for the cataract should be declined, as one eye may be duly sufficient for tolerable vision, and by the operation on one eye, the focus of vision would become dissimilar in the eyes, and the patient derive very little benefit from the operation.

J. B. Serny, M.D., Oculist,

A treatise on local inflammation,
more particularly applied to disease of the eye, 1809.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month. To receive adequate publicity, however, notices of postgraduate courses and meetings should be received at least three months before the date of occurrence.

DEATHS

Dr. LeVal Lund, Los Angeles, California, died January 31, 1954, aged 62 years.

Prof. Maximilian Salzmann, Graz, Austria, died April 18, 1954, aged 91 years.

MISCELLANEOUS

HEADS DEPARTMENT

Appointment of Dr. Fred M. Wilson as chairman of the Department of Ophthalmology in the Indiana University School of Medicine, has been announced by Dean John D. VanNuys. Dr. Wilson will succeed Dr. Robert J. Masters who is relinquishing the chairmanship he has held for the past 11 years to devote full time to his private practice. Active in the expansion of the eye clinic and teaching program for many years, Dr. Masters will continue on the staff as professor of ophthalmology.

MEMORIAL RESEARCH FUND

In recognition of the great interest of Dr. LeGrand H. Hardy in the study of physiologic optics a fund is being established for furthering research in this subject to be known as The Hardy Memorial Research Fund. Contributions may be sent to:

The Hardy Memorial Research Fund
Institute of Ophthalmology
635 West 165th Street
New York 32, New York

EDUCATIONAL LEAFLETS

The Prevention of Blindness Department, Pennsylvania Association for the Blind, has developed and published educational leaflets on various conditions causing blindness. This literature is prepared with the lay public in mind.

For copies of this material, write to:

Prevention of Blindness Department
Pennsylvania Association for the Blind
100 East Price Street
Philadelphia 44, Pennsylvania

GILL MEETING

Attending the recent 27th annual spring congress at the Gill Memorial Eye, Ear and Throat Hospital, Roanoke, Virginia were 275 doctors from 42 states and Canada. There were 23 guest speakers. The 38th annual spring congress will be held from April 4 to 9, 1955.

OCULAR MOTILITY SYMPOSIUM

Ocular motility will be the subject of the New Orleans Academy of Ophthalmology Symposium to be held in New Orleans, Louisiana, January 31-February 4, 1955.

WILMER PROGRAM

On the program of the 13th clinical meeting of the Wilmer Residents Association held recently at the Wilmer Ophthalmological Institute of The Johns Hopkins Hospital, Baltimore, were:

"An etiologic classification of endogenous uveitis," Dr. Alan C. Woods; "Therapeutic keratoplasty for corneal ulcer," Dr. Charles W. Tillett; "Therapeutic corneal transplants," Dr. R. Townley Paton; "Treatment of intermittent exotropia," Dr. Daniel A. Russell, Jr.; "Intravenous nitrogen mustard for retinoblastoma," Dr. Carl Kupfer.

"Results with enucleation, 1944-1952," Dr. L. Harrell Pierce and Dr. Bradford Hardie; "Adrenal steroids in cataract surgery," Dr. John M. McLean; "Orbital reconstruction utilizing temporalis muscle," Dr. Howard Naquin; "Beta radiation cataracts," Dr. William F. Hughes, Jr.; "Peculiar thrombi in the ciliary veins of newborn infants," Dr. Volckherdt M. de Groot and Dr. Jonas S. Friedenwald; "Posterior lip sclerectomy for glaucoma." Dr. Charles E. Iliff and Dr. Joseph S. Haas; "New techniques in extraocular muscle surgery," Dr. Angus L. MacLean.

"A simple method of sclerocorneal suture," Dr. Malcolm W. Bick; "The influence of ACTH and cortisone on absorption of vitreous hemorrhage," Dr. R. A. Schimek and Dr. E. H. Steffensen; "Clinical evaluation of the Haidinger brush phenomenon'," Dr. Louis Sloan and Dr. Howard Naquin; "Symposium: Diamox in ophthalmology," Dr. Jonas S. Friedenwald, Dr. Bernard Becker, Dr. V. Everett Kinsey, Dr. Erik Linner, and Dr. Richard L. Riley.

"The outflow pressure in normal and glaucomatous eyes," Dr. Erik Linner; "Directions of research in diabetic retinopathy: A progress report," Dr. David A. Rosen, Dr. Bernard Becker, Dr. Gertrude Maengwyn-Davies, and Dr. Jonas S. Friedenwald; "Pathogenesis of congenital glaucoma," Dr. A. E. Maumenee; "Studies on radioactive phosphorus in the diagnosis of intraocular pathology," Dr. William C. Owens, Dr. J. H. King, Jr., and Dr. H. J. Wells; "Retinal activity during light and dark adaptation," Dr. Stephen W. Kuffler; "Problems of light threshold measurement in the retina," Dr. Richard FitzHugh.

"The long cane," (movie), Dr. Richard Hoover; "Cataract extraction without an assistant," (movie) Dr. Charles E. Iliff; "Neuro-ophthalmological

clinic," Dr. Frank B. Walsh; "A demonstration of Bassett's stereoanatomy of the orbit and eye," Dr. A. E. Maumenee.

Massachusetts eye and ear alumni meeting

At the recent joint meeting of the New England Ophthalmological Society and the ophthalmological section of the Massachusetts Eye and Ear Alumni Association the following program was given:

"Presentation of cases," Dr. Robert B. Leavelle; "Luxation of the globe," Dr. Bertha Offenbach; "Some hitherto underscribed trephines, automatic and semiautomatic, hand-driven, spring-driven, and electrically driven," Dr. Frederick H. Verhoeff; "Clinical pathologic observations on the corneal endothelium," Dr. A. Ray Irvine, Jr.

Dr. Frank B. Walsh, Baltimore, delivered the annual Howe Lecture. His subject was "A clinical study of several third-nerve lesions."

"Optico-ciliary neuritis," Dr. Irwin T. Mancall; "Intraocular cotton after surgery," Dr. Robert J. Brockhurst; "Experiences with radioactive phosphorus P^{32}," Dr. Edwin B. Dunphy and Dr. Knud K. Dreisler; "Some observations on retinal artery pressure," Dr. David G. Cogan; "A significant case of narrow-angle glaucoma," Dr. Thomas Cavanaugh; "Pathology of subclinical retinal breaks viewed ophthalmoscopically in Eye-Bank eyes," Dr. Samuel T. Adams; "Comparison of water-drinking test and tonography," Dr. Robert R. Trotter; "Ocular mercurialism," Dr. Alfred Kant.

Societies

Chicago society officers

Dr. Justin M. Donegan, Evanston, Illinois, was elected president of the Chicago Ophthalmological Society at its annual meeting. The society has a membership of 228 eye physicians and surgeons from all over the Middle West. Dr. Bertha A. Klien, Chicago, was elected vice-president; Dr. James E. Lebensohn, Chicago, councilor; Dr. Richard C. Gamble, Park Ridge, was re-elected corresponding secretary and Dr. Frank W. Newell, Chicago, was re-elected secretary-treasurer.

German meeting

The Deutsche Gesellschaft fuer Optometrie, Kongressleitung: Carl-Heinz Nitzschke, Berlin-Wilmersdorf, Detmolder Strasse 66 announces that this year its sixth annual congress will convene September 20 to 25, in Berlin. There will be short courses in special fields in optometry as well as lectures and discussions.

Reading meeting

At the 142nd meeting of the Reading (Pennsylvania) Eye, Ear, Nose and Throat Society, the speaker was Irving Lueck, Ph.D., assistant director of ophthalmic research and development, Bausch and Lomb, Rochester, New York. Dr. Lueck presented a blackboard talk on "Practical aspects of optics."

Before dinner a study club was held on hoarseness. The moderator was Dr. Michael J. Penta, Reading. The two instructors were: Dr. Archibald Judd and Dr. Isaac High also of Reading.

Elected to office for next year were: President, Dr. C. W. Hancox, Pottstown; first vice president, Dr. Marvin K. Rothenberger, Allentown; second vice president and president elect, Dr. Gerald Smith, Lancaster; treasurer, Dr. Philip B. Wiest, Reading; secretary, Dr. James H. Parker, Jr., Reading.

Indiana meeting

Guest speakers at the recent meeting of the Indiana Academy of Ophthalmology and Otolaryngology were: Dr. James H. Allen, New Orleans, and Dr. Francis W. Davison, Danville, Pennsylvania.

Ophthalmic Miniature

> And when the evening mist clothes the riverside with poetry, as with a veil, and the poor buildings lose themselves in the dim sky, and the tall chimneys become campanile, and the warehouses are palaces in the night, and the whole city hangs in the heavens, and fairyland is before us—then the wayfarer hastens home; the working man and the cultured one, the wise man and the one of pleasure, cease to understand, as they have ceased to see, and Nature, who for once has sung in tune, sings her exquisite song to the artist alone, her son and master—her son in that he loves her, her master in that he knows her.
>
> J. A. McN. Whistler,
> *Ten O'Clock.*

The Purpose of the Guild

- The aim of the Guild of Prescription Opticians of America is to advance the science of ophthalmic optics through the development of a country-wide ethical optical dispensing service that comprehensively meets the needs of the Eye Physicians and their patients; and to educate the public to the fact that the Eye Physician-Guild Optician type of eye service truly renders the most desirable form of eye care.

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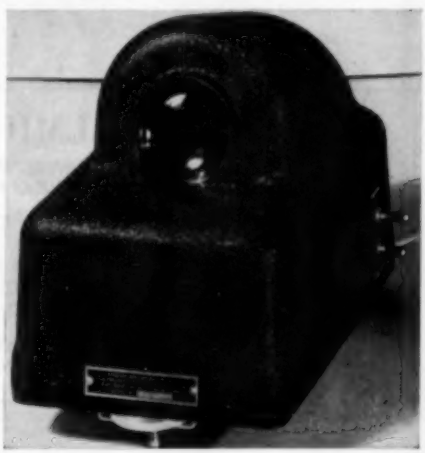

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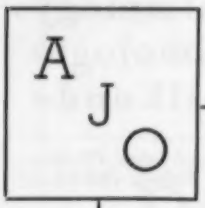

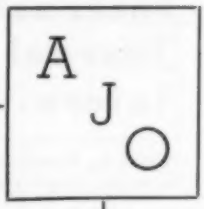

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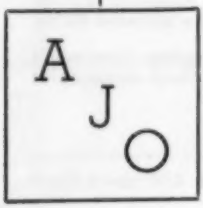

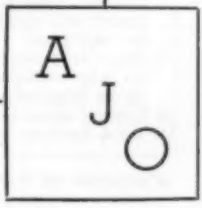

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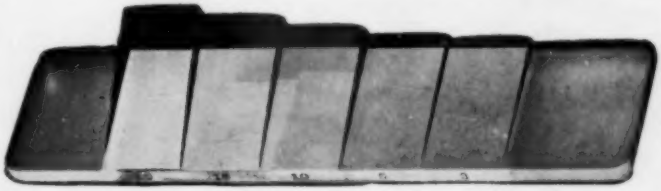

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